VOLUME 45 JUNE 1952 NUMBER 6

Southern Medical Journal

Journal of the Southern Medical Association

Copyright, Southern Medical Association, 1952. Published monthly by the Southern Medical Association, Empire Building, Birmingham 3, Alabama. Annual subscription $10.00. Entered as Second-Class Matter at the Post Office at Birmingham, Alabama, under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized December 20, 1921.

Southern Medical Association, Forty-Sixth Annual Meeting, Miami, Florida, November 10-13, 1952

TABLE OF CONTENTS

Chronic Perforating Carcinoma of the Colon. Clyde A. Stevenson and Arno W. Sommer, Temple, Texas 477

Discussed by Glenn D. Carlson, Dallas, Texas.

Factors Influencing the Prognosis of Cancer of the Colon. Raleigh R. White, Temple, Texas 481

Discussed by Raymond L. Murdoch, Oklahoma City, Oklahoma.

Benign Tumors of the Ureter. W. V. Pierce and W. R. Miner, Covington, Kentucky 485

Discussed by Hugh T. Beacham, New Orleans, Louisiana; Vincent Vermooten, Dallas, Texas.

Medical Uses of Cobalt 60. Herbert D. Kerman, Oak Ridge, Tennessee 495

Discussed by Gilbert H. Fletcher, Houston, Texas; Isadore Meschan, Little Rock, Arkansas; Charles L. Martin, Dallas, Texas; Edwin C. Ernst, St. Louis, Missouri.

Aneurysm of the Ascending Aorta. J. E. Miller, Dallas, Texas 503

Discussed by E. W. Spackman, Fort Worth, Texas.

Some Considerations Regarding Long-Term Rehabilitation of Brain Injuries. Ben L. Boynton and L. A. Leavitt, Houston, Texas 508

Surgical Training for the General Practitioner. Randolph T. Smith, Little Rock, Arkansas 511

Discussed by William J. Fetzer, San Antonio, Texas.

The Coxsackie Viruses: Properties, Immunological Aspects and Role in Human Disease. S. Edward Sulkin, Dallas, Texas 516

Discussed by Thomas W. Farmer, Dallas, Texas; Robert E. Blount, Fort Sam Houston, Texas.

Respiratory Acidosis and Alkalosis. Fontaine S. Hill, Memphis, Tennessee 521

Prolonged Vomiting as a Cause of Potassium Deficiency. Burton A. Shatz and Frank J. Catanzaro, St. Louis, Missouri 525

Discussed by George T. Harrell, Winston-Salem, North Carolina; E. E. Muirhead, Dallas, Texas.

Attenuated Virus in Autogenous Blood Serum as a Therapeutic Agent in Herpes Zoster. Charles P. Bondurant, Oklahoma City, Oklahoma 529

Discussed by Thomas W. Murrell, Richmond, Virginia; Howard Hailey, Atlanta, Georgia; Onis G. Hazel, Oklahoma City, Oklahoma; C. Ferd Lehmann, San Antonio, Texas; Thomas B. Hall, Kansas City, Missouri; D. Truett Gandy, Houston, Texas.

Carcinoma of Ovary: Newer Aspects. Wm. F. Guerriero, J. W. Tabler and Charles Bruce, Dallas, Texas 533

Discussed by Lee F. Turlington, Birmingham, Alabama; John C. Weed, New Orleans, Louisiana.

Continued on next page

TABLE OF CONTENTS
Continued

Public Health Aspects of Heart Disease. Alfred W. Harris, Dallas, Texas 538
Discussed by Wm. S. Brumage, Austin, Texas.

Treatment of Mass Burns. B. W. Haynes, Jr., Houston, Texas 545

Industrial Hygiene Problems as Seen by a Workman Compensation Carrier. Henry T. Herndon, Dallas, Texas 551
Discussed by Lewis William Fetzer, Dallas, Texas; Carl A. Nau, Galveston, Texas.

The Clinical Use of the Barbiturates. Oliver F. Bush, Dallas, Texas 553

Cortisone in Acute Rheumatic Carditis. John A. Boone and Mylnor W. Beach, Charleston, South Carolina 556

Pernicious Anemia Complicated by Acute Granulocytic Leukemia: A Case Report. R. W. Talley, J. E. Doherty and C. F. Shukers, Little Rock, Arkansas 559

Treatment of Acute Hematogenous Osteomyelitis in Children. Blair E. Batson, Nashville, Tennessee 562
Discussed by B. F. Boylston, Houston, Texas.

Pathology of Abnormal Uterine Bleeding. Richard A. Street, Jr., Vicksburg, Mississippi 569
Discussed by John M. Fleming, Spartanburg, South Carolina.

EDITORIALS 574
- Mumps Diagnosis
- Cause of Hypotension after Severe Burns
- Manganese in Digestion
- Twenty-Five Years Ago

BOOK REVIEWS 577

BOOKS RECEIVED 579

SOUTHERN MEDICAL NEWS 580

The Tulane University
SCHOOL OF MEDICINE
DIVISION GRADUATE MEDICINE

Basic Science Course in Ophthalmology, Twelve months, beginning . . July 1, 1952

Basic Science as Applied to Orthopedics, Five months, beginning . . February 1, 1953

Tropical Medicine and Public Health, leading to the degree of Master of Public Health and Master of Public Health (Tropical Medicine), Nine months beginning . . September, 1952

Electrocardiography . . December 1-13, 1952

Ocular Pathology . . . . December 1-6, 1952

Surgery and Traumatology for General Practitioners . . January 12-17, 1953

Individually arranged long term courses.

For detailed information write

DIRECTOR

1430 Tulane Avenue New Orleans 12, La.

NEW BOOK

Surgical Gynecology

Including Important Obstetric Operations

By J. P. GREENHILL, M.D., 350 pages, $8.50

This volume is an innovation in surgical literature. Prepared for all who must perform gynecologic surgery, this handbook presents simply but vividly today's standard gynecologic operations, plus important obstetric operations and such procedures as herniotomy, appendectomy, surgery of the bowel, bladder and ureter, etc., which, while not strictly gynecologic operations, must nonetheless be done frequently by the gynecologic surgeon.

The 492 superb line drawings on 101 full-page plates are all original. In the unique format, all pictures are placed on right-hand pages, with complete, related text always facing on the left. From incision to closure, each operation is graphically shown step by step.

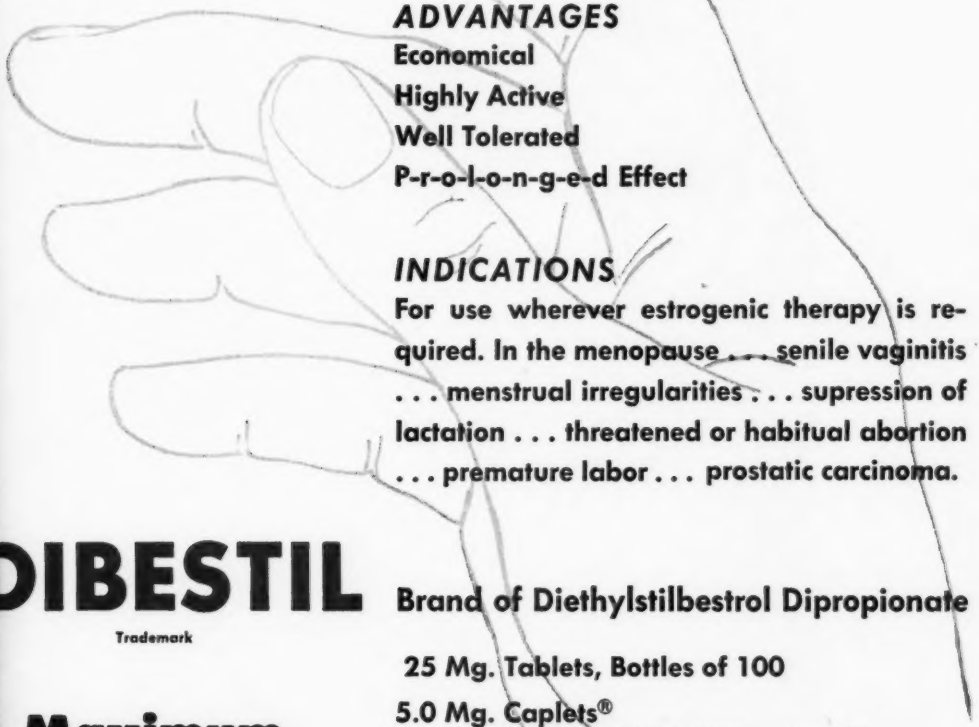
SEND ORDERS TO

J. A. MAJORS COMPANY

NEW ORLEANS 12 DALLAS 1 ATLANTA 3

Vol.

Complete ORAL ESTROGENIC THERAPY AT YOUR FINGERTIPS



ADVANTAGES

Economical
Highly Active
Well Tolerated
P-r-o-l-o-n-g-e-d Effect

INDICATIONS

For use wherever estrogenic therapy is required. In the menopause . . . senile vaginitis . . . menstrual irregularities . . . supression of lactation . . . threatened or habitual abortion . . . premature labor . . . prostatic carcinoma.

DIBESTIL

Trademark

Brand of Diethylstilbestrol Dipropionate

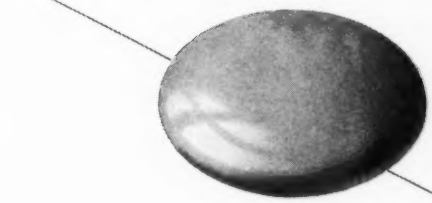
Maximum Dosage Flexibility

25 Mg. Tablets, Bottles of 100
5.0 Mg. Caplets®
Bottles of 100, 250 and 1000
1.0 Mg. Caplets
Bottles of 100, 500 and 1000
0.5 Mg. Caplets
Bottles of 100, 500 and 1000
0.2 Mg. Caplets
Bottles of 100, 500 and 1000

BREON

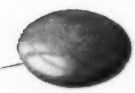
George A. **Breon** & Company

1450 BROADWAY NEW YORK 18, N. Y.



new convenience

in broad-spectrum therapy

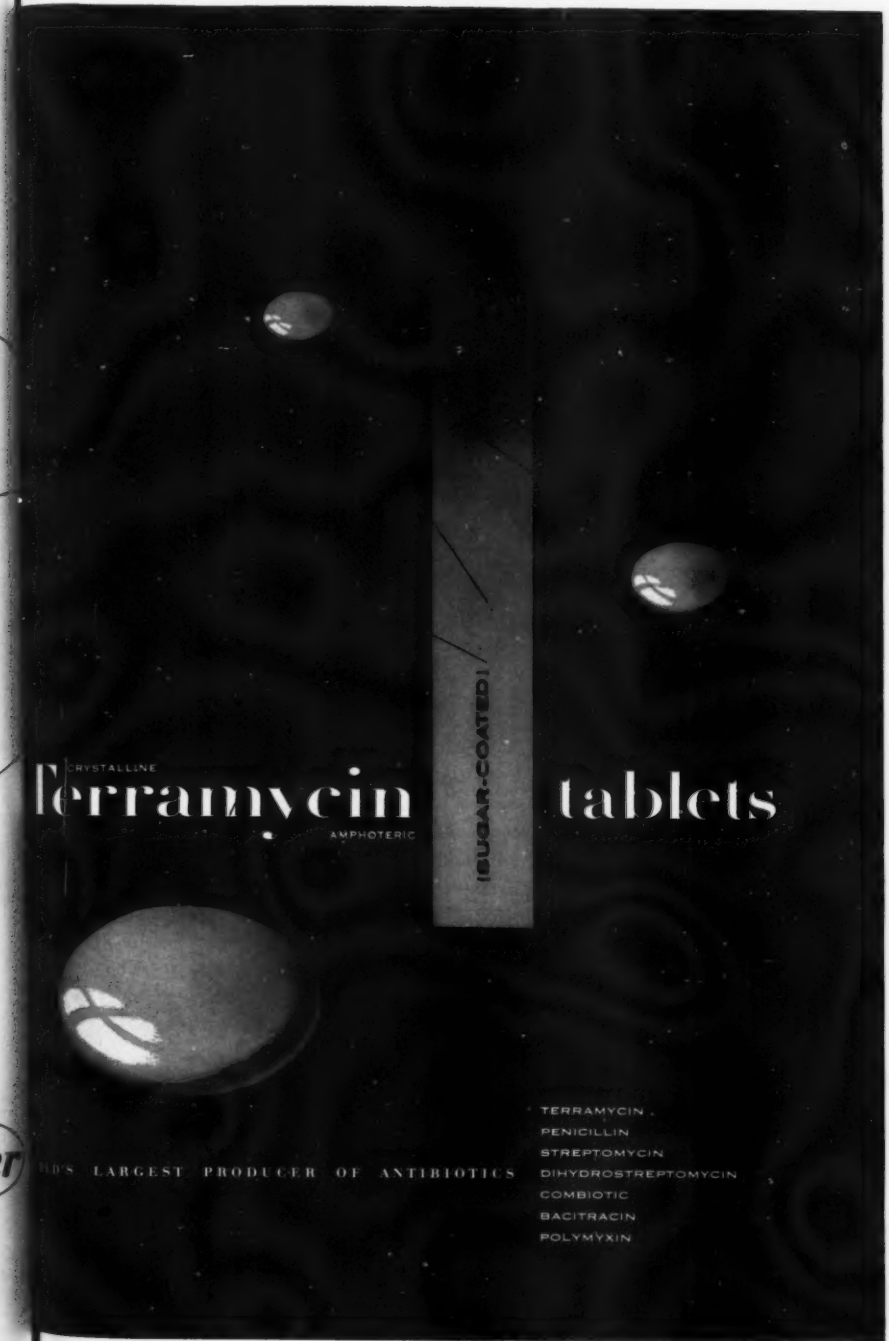


Easily swallowed, sugar-coated Terramycin Tablets introduce new flexibility in prolonged courses of administration and are particularly suited to effective, well tolerated therapy among patients preferring tablets to other oral forms.

Supplied: 250 mg. tablets, bottles of 16 and 100; 100 mg. and 50 mg. tablets, bottles of 25 and 100.

ANTIBIOTIC DIVISION, CHAS. PFIZER & CO., INC.
Brooklyn 6, N.Y.

Pfizer


CRYSTALLINE
Terramycin
AMPHOTERIC
SUGAR-COATED
tablets
TERRAMYCIN
PENICILLIN
STREPTOMYCIN
DIHYDROSTREPTOMYCIN
COMBIOTIC
BACITRACIN
POLYMYXIN
LD'S LARGEST PRODUCER OF ANTIBIOTICS

From among all antibiotics, Orthopedic Surgeons often choose

New aureomycin minimal dosage for adults—four 250 mg. capsules daily, with milk.

AUREOMYCIN

Hydrochloride Crystalline

because

Aureomycin, following oral administration, diffuses rapidly into the skeletal and structural tissues of the body.

Aureomycin exhibits little tendency to favor the development of resistant bacterial strains.

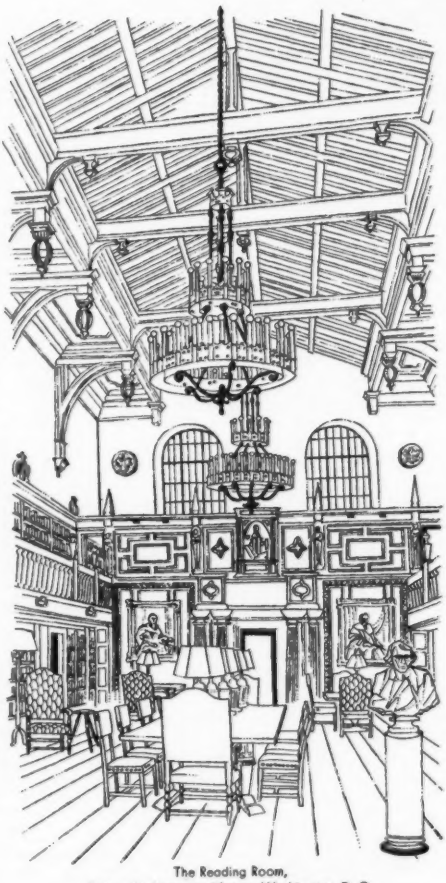
Aureomycin in daily repeated small dosage gives satisfactory serum levels, and may be continued over a long period.

Aureomycin has been reported to be clinically effective against susceptible organisms in the following conditions frequently seen by the orthopedic surgeon:

Suppurative Arthritis • Osteomyelitis
Infected Compound Fractures • Osteitis
Brucella Arthritis • Periostitis

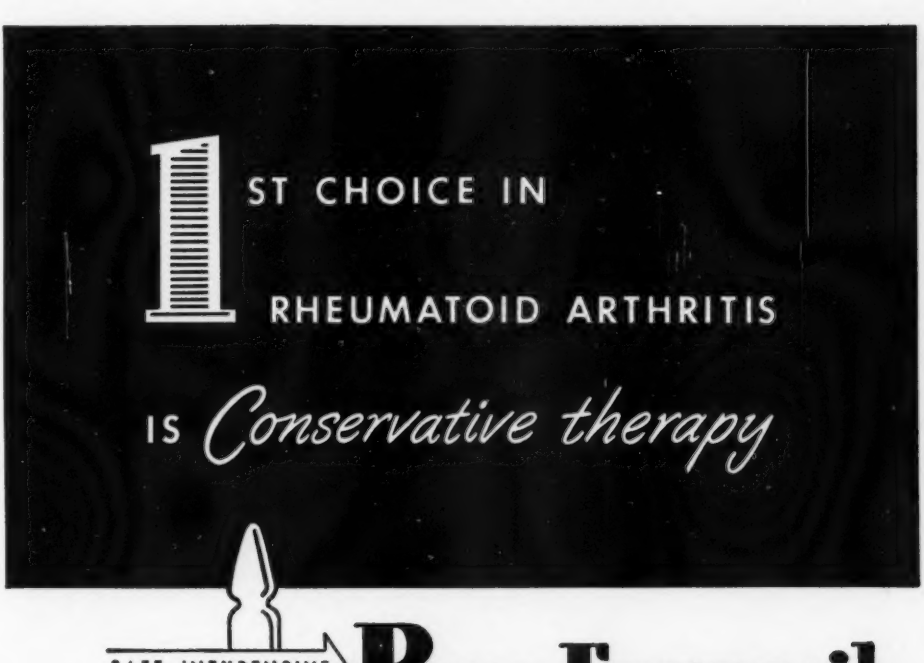
Throughout the world, as in the United States, aureomycin is recognized as a broad-spectrum antibiotic of established effectiveness.

Capsules: 50 mg.—Bottles of 25 and 100; 250 mg.—Bottles of 16 and 100. *Ophthalmic:* Vials of 25 mg. with dropper; solution prepared by adding 5 cc. of distilled water.



The Reading Room,
Folger-Shakespeare Library, Washington, D. C.

LEDERLE LABORATORIES DIVISION
AMERICAN Cyanamid COMPANY
30 Rockefeller Plaza, New York 20, N. Y.



For more than 16 years clinicians have successfully employed *Ray-Formosil* to control the distressing and disabling symptoms of rheumatoid arthritis.

While *Ray-Formosil* seldom produces the immediate dramatic effects of hormonal preparations, it is consistently effective when used adequately, and it obviates the two serious disadvantages of "wonder drug" therapy, namely, severe toxicity and high cost. As first-choice conservative therapy, *Ray-Formosil* provides the opportunity to effect symptomatic relief without danger of precipitating the undesirable physiologic responses characteristic of hormonal medication.

An analysis of nearly 4,000 recent case histories from the files of 36 clinicians revealed that 85% of rheumatoid arthritics experienced relief of pain, swelling and joint inflammation following a course of *Ray-Formosil* injections. None experienced any untoward side effects attributable to therapy regardless of the degree of clinical response.

Only 36¢ a treatment ampul, *Ray-Formosil* therapy is inexpensive—an additional and important advantage to both the physician and the patient.

Dosage: 2 cc. injected intramuscularly *in the region of the affected parts* at 2- to 5-day intervals for several weeks, then 2 cc. once weekly.

Supplied in 2-cc. ampuls in boxes of 25 ($9.00), 50 ($16.50), and 100 ($30.00).

Available through your usual source of pharmaceuticals or direct from the manufacturer.

RAYMER PHARMACAL COMPANY

Pharmaceutical Manufacturers
Jasper and Willard Streets, Philadelphia 34, Pa.

SERVING THE MEDICAL PROFESSION FOR NEARLY A THIRD OF A CENTURY

patients
who
"can't take"
aspirin . . . may take

SILMIDATE Trademark

for efficient
pain relief
without
unwanted
side effects

SALICYLAMIDE . . . 250 mg. (4 gr.) Safer, more rapid, more effective, and more useful than ordinary salicylates. Can be given in larger doses without danger of gastric irritation or prolongation of prothrombin time.

CALCIUM SUCCINATE . . . 200 mg. (3 gr.) Aids in maintaining normal tissue respiration and further decreases any likelihood of salicylate toxicity.

ASCORBIC ACID . . . 25 mg. (5/12 gr.) Helps to normalize blood vitamin C level, prevent its depletion by salicylate, ward off capillary fragility, and aid healing processes.

SUPPLIED: Bottles of 100 and 500.

SILMIDATE* is indicated for acute rheumatic fever, arthralgias, myalgias, certain types of arthritis, analgesia after tonsillectomy and tooth extractions (without risk of hemorrhage), and wherever salicylate analgesia is indicated.

CCH

CHARLES C. HASKELL & CO., INC., RICHMOND, VIRGINIA

*Trademark of Charles C. Haskell & Co., Inc.

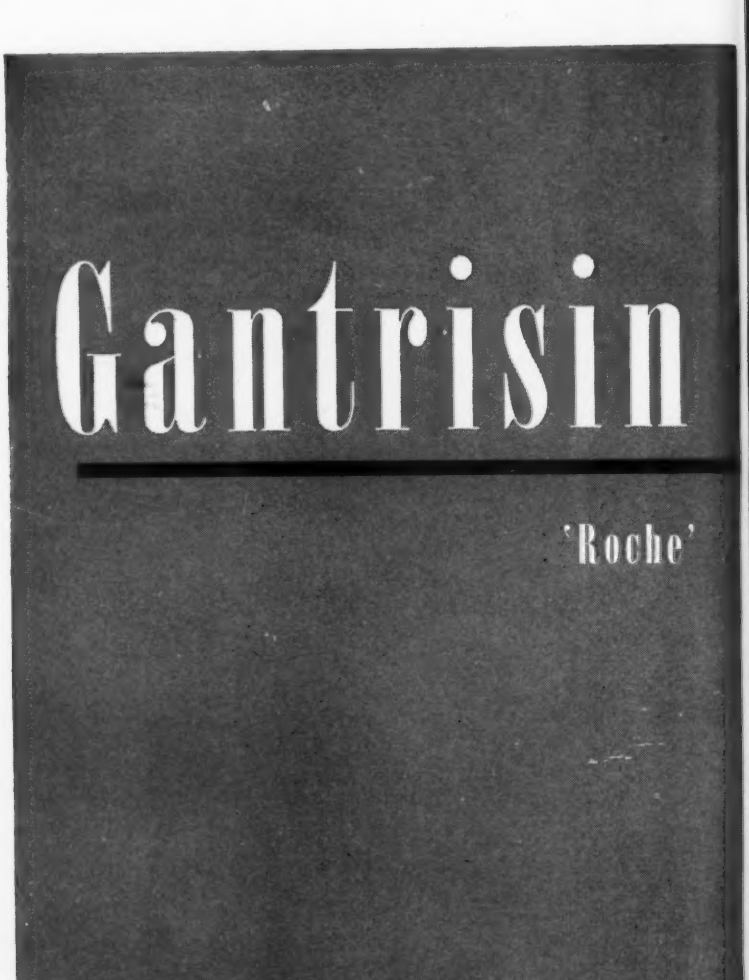
In Dermatitis

CREMACAL

Protects without bandaging

2 oz. Tubes Greaseless

NUMOTIZINE, Inc. 900 N. Franklin Chicago, Illinois, U. S. A.


Gantrisin
'Roche'

antibacterial action plus...

■ **greater solubility**

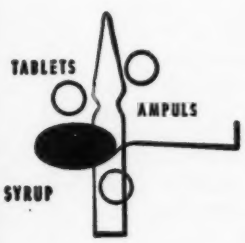
Gantrisin is a sulfonamide so soluble that there is no danger of renal blocking and no need for alkalinization.

■ **higher blood level**

Gantrisin not only produces a higher blood level but also provides a wider antibacterial spectrum.

■ **economy**

Gantrisin is far more economical than antibiotics and triple sulfonamides.



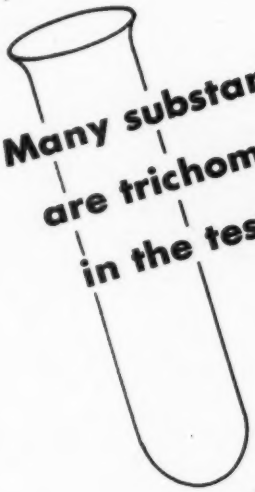
■ **less sensitization**

Gantrisin is a single drug—not a mixture of several sulfonamides—so that there is less likelihood of sensitization.

GANTRISIN®—brand of sulfisoxazole
(3,4-dimethyl-5-sulfanilamido-isoxazole)

HOFFMANN-LA ROCHE INC.

Roche Park • Nutley 10 • New Jersey



Many substances are trichomonacidal in the test tube .... but

Here is dependable therapeutic efficacy in trichomoniasis

VAGISOL
SUPPOSITABS

Nonstaining, odorless, nonirritant, each Vagisol Suppositab supplies:

Phenyl Mercuric Acetate	3.0 mg. (0.046 grain)
Tyrothricin, N.F.	0.5 mg. (0.008 grain)
Succinic Acid	12.5 mg. (0.193 grain)
Sodium Lauryl Sulfate	3.0 mg. (0.046 grain)
Papain	25.0 mg. (0.385 grain)
Lactose	q.s.

Clinical cure in trichomonas vaginitis—proved by smear and culture—is the rule when Vagisol Suppositabs are employed. These tablet-shaped suppositories provide a powerful germicidal-antibiotic approach which promptly controls the patient's characteristic discomfort and leads to complete eradication of the parasite. The presence of succinic acid and lactose is conducive to the growth of the normal Doederlein bacillus, while papain and sodium lauryl sulfate encourage penetration of the medication into the mucosal folds.

Vagisol Suppositabs, in addition to being specifically indicated in trichomonas vaginitis, are also valuable in the management of other vaginal and cervical infections. The usual course of treatment consists of one suppositab inserted high in the vagina twice daily for 30 days. Available through all pharmacies, in bottles of 36.

SMITH-DORSEY • Lincoln, Nebraska
A Division of THE WANDER COMPANY

A *Dorsey* PREPARATION

In a matter of minutes...

GRATIFYING RELIEF

From distressing

Urogenital Symptoms

In a matter of minutes, the local analgesic action of PYRIDIUM safely allays burning, dysuria, urgency, and frequency which often accompany cystitis, prostatitis, urethritis, and pyelonephritis.

PYRIDIUM is compatible with crystalline dihydrostreptomycin sulfate, penicillin, the sulfonamides, or other specific therapy, and is frequently administered together with one of these agents to provide the dual approach of symptomatic relief and corrective action.

PYRIDIUM®

(Brand of Phenylazo-diamino-pyridine HCl)

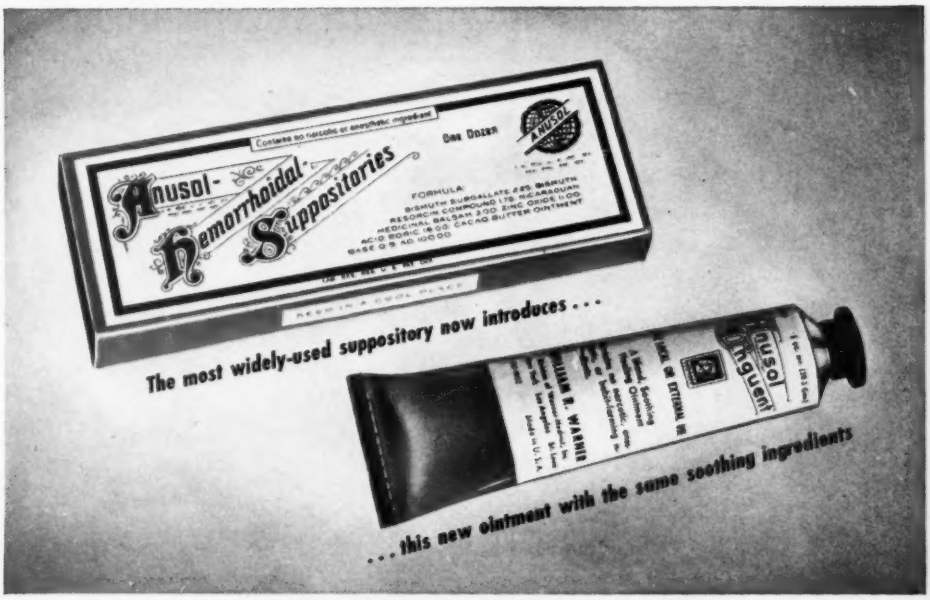
PYRIDIUM is the registered trade-mark of Nepera Chemical Co., Inc. for its brand of phenylazo-diamino-pyridine HCl. Merck & Co., Inc. sole distributor in the United States.

MERCK & CO., INC.

Manufacturing Chemists

RAHWAY, NEW JERSEY

In Canada: MERCK & CO. Limited—Montreal


Anusol-
Hemorrhoidal
Suppositories
The most widely-used suppository now introduces . . .
. . . this new ointment with the same soothing ingredients

Your patients will be grateful for the itch-relief they get

NEW... Anusol Unguent for external use

Patients with hemorrhoidal and similar conditions invariably have a persistent itch in the anal sector. To relieve this trouble, Anusol Unguent is now available.

Containing the same ingredients as the Suppositories, this new ointment provides prompt, prolonged relief. It is safe, convenient, stable, and not smelly or sticky.

You may prescribe Anusol Unguent with the same confidence you have always had in Anusol Suppositories.

Anusol Unguent is supplied in 1-oz. tubes. Samples and literature on request.

MANY SKIN AILMENTS RESPOND TO ANUSOL

Prompt relief from irritation, burning and itching is afforded by Anusol Unguent. It reduces inflammation, congestion and swelling. Its mild, astringent, antiseptic action hastens healing. General indications:

- Acne vulgaris
- Herpes simplex
- Drug rashes
- Ivy poisoning
- Sunburn
- Burns, abrasions, scalds

Anusol®
SUPPOSITORIES • UNGUENT

WILLIAM R. WARNER
DIVISION OF WARNER-HUDNUT, INC. • NEW YORK 11, N. Y.

1952

NEW AID FOR

MOBILIZING THE DEFENSES OF

THE MAN WHO DEVELOPS *ULCER*

ACCEPTED COUNCIL ON PHARMACY AND CHEMISTRY AMERICAN MEDICAL ASSOCIATION

To acquire an ulcer, the patient—*somehow* overcomes the powerful defense mechanisms constantly working to maintain the normal integrity of gastrointestinal mucosa. To heal the ulcer, it is necessary to mobilize and implement these mechanisms as promptly and effectively as possible. Robalate, the new Robins' preparation for modern ulcer therapy, helps accomplish this by providing rapid, prolonged neutralization of hyperacidity, and a protective coating over the ulcer crater. It quickly relieves ulcer pain. It causes: *no acid rebound . . . no alkalosis . . . no disturbance in electrolyte balance.* Particularly noteworthy: It is free from chalky, gritty taste. To help the ulcer help itself, depend on Robalate.

A. H. ROBINS COMPANY, INC.
RICHMOND 20, VIRGINIA

Multiple chronic gastric ulcers. Completely disappeared under antacid-demulcent therapy.

TABLETS

ROBALATE® Robins

(Dihydroxy Aluminum Aminoacetate, N.N.R.)

For — freedom from ulcer pain . . . — freedom for the lesion to heal . . . — freedom from gastric hyperacidity . . . — freedom from chalky, gritty antacids . . .

Accepted by the Council on Pharmacy and Chemistry of the American Medical Association

YESTERDAY TODAY

The "Great Debate"

Men also spoke of a *great debate* 'way back in 1878. It concerned the coinage of silver and the retirement of greenbacks. Financial stability seemed at stake. Debate was heated, feelings ran high, many men were disturbed about the future. • Yet, despite these problems and perplexities, in 1878 the pharmaceutical house of A. H. Robins Company was founded . . . and dedicated to principles about which there could be no debate: Robins' products were to be soundly formulated . . . research-proven . . . and promoted *exclusively* to the medical profession. • From that day to this, the firm has grown many hundredfold . . . *yet never at the expense of those principles.* The introduction of each new Robins' product has been another milestone in the steady progress of a house and a policy that, for nearly seventy-five years, have grown in the service of American Medicine.

A. H. ROBINS CO., INC.
RICHMOND 20, VIRGINIA

Robins

ETHICAL PHARMACEUTICALS OF MERIT SINCE 1878

two sides to this story...

When spasm of the sphincter of Oddi (left) is relaxed (right), bile pours into the duodenum.

In many biliary conditions, combined hydrocholeretic and antispasmodic therapy is indicated for best results to flush the bile ducts with a greater volume of bile and to relax spasm in the sphincter of Oddi.

Cholan *hmb*

Dehydrocholic acid, the most potent hydrocholeretic known, stimulates copious secretion of thin, free-flowing bile...increases volume output by as much as 190%... is the least toxic of any bile salt, bile acid, or their derivatives.

*Homa*tropine *methyl*bromide and phenobarbital, by their synergistic spasmolytic-sedative actions, relax spasm of the sphincter of Oddi—and neutralize hypertonic dysfunction of the biliary tract.

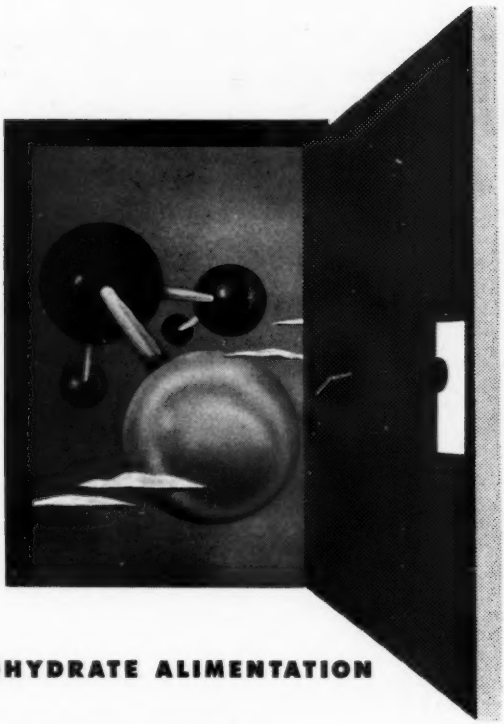
Cholan-HMB contains, in addition to dehydrocholic acid-Maltbie, 250 mg. (3¾ gr.) per tablet, the spasmolytic *homa*-tropine *methyl*bromide 2.5 mg. (1/24 gr.), and phenobarbital 8 mg. (⅛ gr.).

stimulation of free-flowing bile

relaxation of spasm in sphincter of Oddi

MALTBIE LABORATORIES, INC., Newark 1, N. J.

MALTBIE... *first to develop American process for converting crude viscous ox-bile into chemically pure dehydrocholic acid.*



Opening the door to . . .

INCREASED CARBOHYDRATE ALIMENTATION

10% *Travert*® SOLUTIONS
(INVERT SUGAR)

- *for twice the calories of 5% dextrose*
- *in equal infusion time*
- *with no increase in fluid volume*

With *10% Travert* solutions, a patient's carbohydrate needs can be more nearly satisfied within a reasonable time with no increase in fluid volume or vein damage.

Travert solutions are sterile, crystal clear, colorless, non-pyrogenic and non-antigenic. They are prepared by the hydrolysis of cane sugar and are composed of equal parts of D-glucose (dextrose) and D-fructose (levulose).

Travert solutions are available in water or saline in 150 cc., 500 cc., 1000 cc. sizes.

For the treatment of potassium deficiency, *10% Travert* solutions with 0.3% potassium chloride are also available in 1000 cc. containers.

Travert is a trademark of BAXTER LABORATORIES, INC.

products of

BAXTER LABORATORIES, INC.

Morton Grove, Illinois • Cleveland, Mississippi

DISTRIBUTED AND AVAILABLE ONLY IN THE 37 STATES EAST OF THE ROCKIES (except in the city of El Paso, Texas) THROUGH

AMERICAN HOSPITAL SUPPLY CORPORATION

GENERAL OFFICES • EVANSTON, ILLINOIS

RETAFEN *Ointment*

with Hexachlorophene and other effective medicaments

For minor skin irritations

ANTIPRURITIC • ANTIBACTERIAL • ANTIFUNGAL

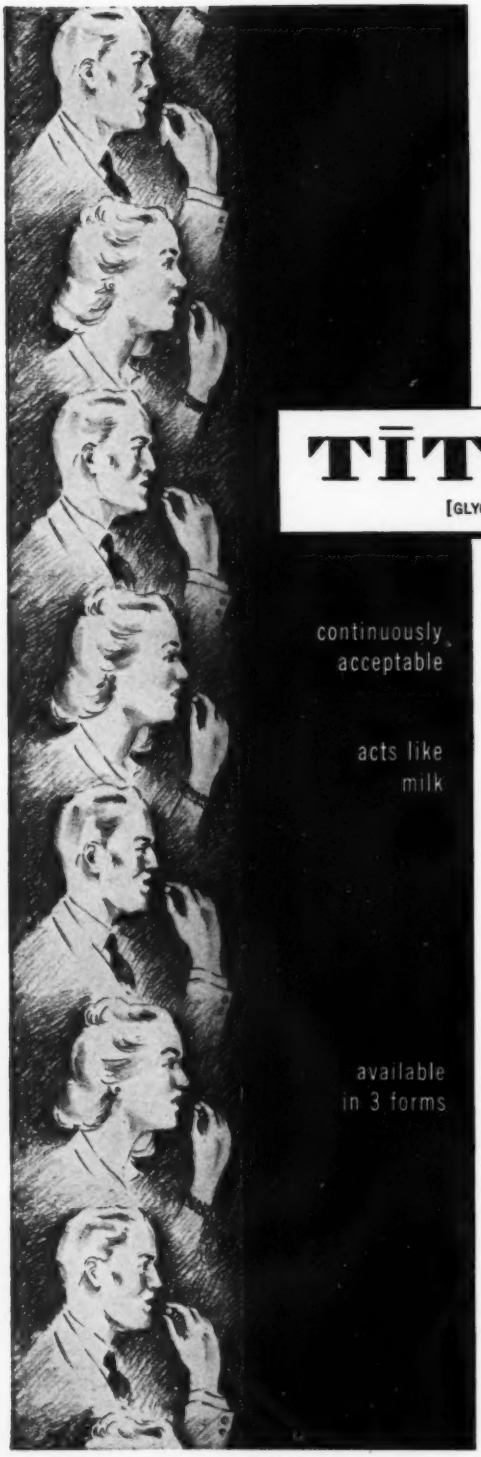
Hexachlorophene 1%, Acid Carbolic 0.9%, Resorcinol 1%, Oil of Tar Rectified 0.5% and Zinc Oxide 4% in a specially prepared, perfumed, polyethylene glycol base—readily releasing the active ingredients at the site of administration, non-irritating, easily washable and non-staining.

Supplied in 15 Gm. (½ oz.) tubes, individually cartoned, and 3¾ oz. jars.

Also available: Retafen Liquid in 2 fluidounce bottles.

VB

VANPELT & BROWN, Inc. *Pharmaceutical Chemists* **RICHMOND 4, VA.**



your patient
will not tire
of taking...

TĪTRALAC
TRADEMARK
[GLYCINE AND CALCIUM CARBONATE]

an effective antacid

continuously acceptable

TĪTRALAC's "just right" mint flavor and smooth texture ensure continuous acceptance.

acts like milk

TĪTRALAC's precise proportions of glycine and calcium carbonate provide a buffering action singularly like that of whole milk.

No systemic alkalosis or acid rebound... free from acid-generating sugars. Especially useful in milk-sensitive patients or where weight gain is undesirable.

available in 3 forms

TĪTRALAC* Tablets.....Boxes of 40, bottles of 100 and 1000
TĪTRALAC Powder.....Jars of 4 oz.
TĪTRALAC Liquid..Bottles of 8 fl. oz.

*Trademark of Schenley Laboratories, Inc.
U. S. Pat. No. 2,429,596
©Schenley Laboratories, Inc.

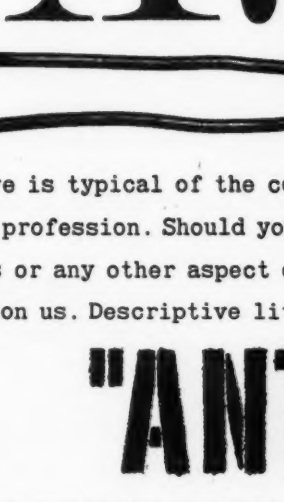
schenley

SCHENLEY LABORATORIES, INC.
LAWRENCEBURG, INDIANA

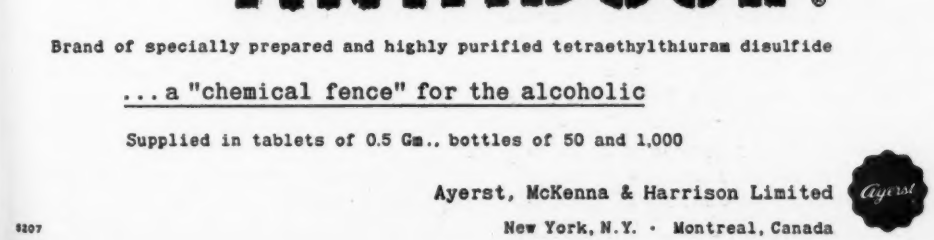
No. 2 of a series

In the treatment of alcoholism with "Antabuse"...

Q. If the patient fails to develop a satisfactory reaction to the drinking trial, should dosage be increased?



A. No. The initial dosage should be continued for one or two more weeks, at which time a drinking trial is likely to produce the desired reaction.



The above is typical of the countless questions received from the medical profession. Should you require further information regarding this or any other aspect of "Antabuse" therapy, please feel free to call on us. Descriptive literature is available on request.

"ANTABUSE"®

Brand of specially prepared and highly purified tetraethylthiuram disulfide

...a "chemical fence" for the alcoholic

Supplied in tablets of 0.5 Gm., bottles of 50 and 1,000

Ayerst, McKenna & Harrison Limited

New York, N.Y. · Montreal, Canada

8207

Clinical Results* with Banthine® Bromide

(Brand of Methantheline Bromide)

22 Published Reports Covering Treatment of 1443 Peptic Ulcer Patients with Banthine

Comprising the reports published in the literature to date which give specific facts and figures of the results of treatment

AUTHORS	No. of Patients	Chronic, Resistant to Other Therapy	TYPES OF ULCERS				RELIEF OF SYMPTOMS (Chiefly Pain)				Surgery or Complications[2]	Side Effects Requiring Discontinuance of Drug[1]	EVIDENCE OF HEALING			
			Duodenal	Jejunal	Stomal	Gastric	Good	Fair	Poor	No Report			Complete	Moderate	None	No Report
Grimson, Lyons, Reeves	100	100	93	7			80	11	4		5		47		19	29
Friedman	15	15	14			1	5		4	[3]			2			13
Bochgaard, Nielsen, Bang, Grueland, Tobiassen	26	26	21			5	16	4	6				8	6	12	
McHardy, Browne, Edwards, Marek, Ward	162		162				136	12	11		3	1	14	9	7	129
Segal, Friedman, Watson	34	34	34[4]				14	13			7	2	5		8	14
Brown, Collins	117	99	117				97	7	8		5	8	55	9	8	40
Asher	77		65		7	5	52	9	16			16		9	21	47
Rodriguez de la Vega, Reyes Diaz	5	4	5				4		1					3	2	
Winkelstein	116	116	102	8		6	102		14				53		18	45
Hall, Hornisher, Weeks	18	18	18				11		1	[3]			18			
Maier, Meili	38	38	24			14[5]	27	7	4[7]				10	2	5	21
Meyer, Jarmon	25	18	25				21		4							25
Poth, Fromm	37	37	37				33	3	1				33	3	1	
Plummer, Burke, Williams	41	41	41				36		5				38		3	
McDonough, O'Neil	104	100	104				63	10	31			11	4		11	89
Broders	60	60	58		1	1	35	19	6				10	1	49[8]	
Legerton, Texter, Ruffin	11		11				11									11
Holoubek, Holoubek, Langford	76	69	76				35	27	10		4	10	26		10	36
Ogborn	42		39	2		1	42[9]									42
Shaiken	48	48	48				33	10	3		2		33	10	3	
Johnston	145	145	145				143		2			2	143		2	
Rossett, Knox, Stephenson	146		141			5	146					4[10]	53			93
TOTALS	1443	988	1380	17	8	38	1142	132	131	12	36	54	532	52	179	634
PERCENTAGES		67.8	95.6	1.2	0.6	2.6	81.3	9.4	9.3		3.7		70.5	6.6	22.9	

1. Not included in tabulations.
2. Included in "Relief of Symptoms" as "Poor" and in "Evidence of Healing" as "None."
3. Four had no symptoms when Banthine therapy was begun.
4. Of which seven were penetrative lesions and five partially obstructive.
5. No symptoms were present in four.
6. Two with symptoms only; no demonstrable ulcer.
7. Three were psychopathic patients and one had a ventricular ulcer of the lesser curvature.
8. Roentgen findings after treatment period of two weeks; forty-seven had duodenal deformity.
9. All returned to work within a week.
10. In these four, after relief of symptoms, Banthine was discontinued because of urinary retention.

During the past two years, more than 200 references to Banthine therapy in peptic ulcer and other parasympathotonic conditions have appeared in medical literature. Of these reports, 22 have presented specific facts and figures on the results of treatment in a total of 1,443 peptic ulcer patients, 67.8 per cent of whom were reported as chronic or resistant to other therapy. These results are tabulated above and show:

"Good" relief of symptoms was obtained in 81.3 per cent of the 1,405 patients on whom reports were available.

"Complete" evidence of healing was obtained in 70.5 per cent of the 883 patients on whom reports were available.

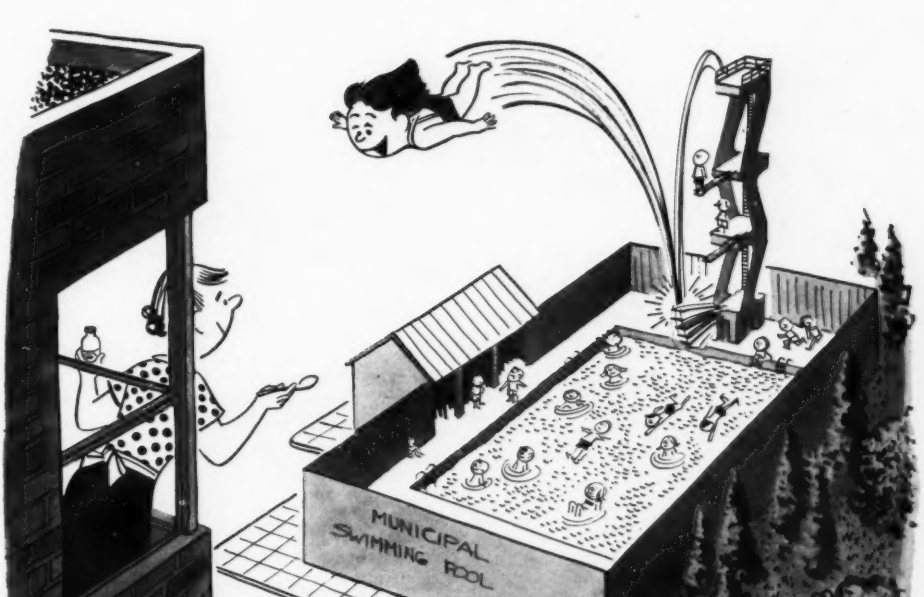
In all but 9.7 per cent, relief of pain was "good" or "fair." In all but 22.9 per cent, evidence of healing was "complete" or "moderate."

During treatment, 26 patients required surgery or developed complications other than ulcer which required discontinuance of the drug before results could be evaluated.

Of the remaining 1,417 patients, only 3.7 per cent experienced side effects sufficiently annoying to require discontinuance of the drug.

*Volume containing complete references, with abstracts of 39 additional reports, will be furnished on request by

G. D. SEARLE & Co., P. O. Box 5110, Chicago 80, Illinois.



She's heard the call for **Vi-Daylin**

(Homogenized Mixture of Vitamins A, D, B_1, B_2, B_{12}, C and Nicotinamide Abbott)

YOUNGSTERS smack their lips at the sight of tempting, yellow-honey VI-DAYLIN, often ask for more when they taste its delicious lemon-candy flavor. Children take it without coaxing, right from the spoon. Here is acceptability—plus.

B_{12} Content Now Tripled . . .

But glance at its potent formula. Each 5-cc. spoonful of VI-DAYLIN now contains 3 mcg. of vitamin B_{12}—three times as much as before—as well as recommended daily allowances of six other essential vitamins. Here, too, is sound vitamin therapy.

No fear of spoilage with VI-DAYLIN—even in thrifty 1-pint sizes—for VI-DAYLIN is stable for as long as two years without refrigeration. Leaves no fishy odor or resistant stains, can be mixed with milk or other foods for infants.

Improved formula

Each 5-cc. teaspoonful of VI-DAYLIN contains:

Vitamin A	3000 U.S.P. units
Vitamin D	800 U.S.P. units
Thiamine Hydrochloride	1.5 mg.
Riboflavin	1.2 mg.
Ascorbic Acid	40 mg.
Vitamin B_{12} Activity (by microbiological assay)	3 mcg.
Nicotinamide	10 mg.

In 90-cc., 8-fluidounce and 1-pint bottles at all pharmacies.

Abbott

Unmatched for Clinical Efficacy

. . . IN DERMATOSES WITH ALLERGIC COMPONENTS

Neurodermatitis (Circumscripta as well as Disseminata)
Urticaria
Papular Urticaria
Allergic Rashes
Allergic Eczematous Dermatitis
Atopic Dermatitis
Dermatitis Venenata
Psoriasis with Allergic Component (as in local bacterial sensitization)
Idiopathic* and secondary Pruritus Ani, Vulvae, and Senilis.

A combination of pyrilamine maleate, 2 per cent, and an extract of carefully selected crude coal tar, derived by an exclusive process of fractionation (Tarbonis brand), 5 per cent, in an emulsified hydrophylic base, non-greasy and clean in application.

●

Available on prescription through all pharmacies and for dispensing and hospital purposes through Physicians' and Hospital Supply Houses, in 2 oz. and 1 lb. jars.

IN dermatoses with allergic components the topical application of Histar may be relied upon to counteract the histamine released into the involved tissues, overcome the effects of the offending allergen, and relieve promptly the attending torment.[1,2] The contained antihistaminic agent, pyrilamine maleate, in spite of its high efficacy is notably low in toxicity—skin irritations and reactions are virtually never encountered.[3,4] Hence Histar has proved far superior to ordinary antihistaminic ointments.

The special tar extract in Histar owes its high clinical value to three excellent therapeutic properties: It is decongestant, anti-inflammatory, and potently antipruritic.

In Histar, the two contained therapeutic agents appear to potentiate each other in a synergistic action which may well be termed physiologic.

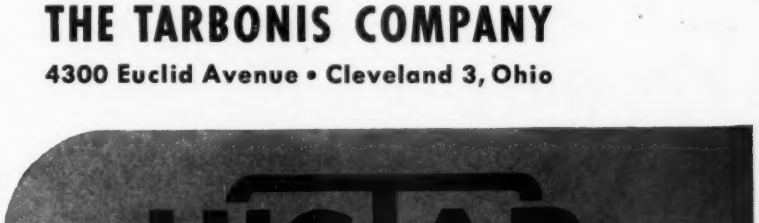
Physicians are invited to use the coupon for comprehensive literature and samples.

References

1. Walters, J. D., and Gilman, R. L.: A Combination of Tar and Antihistaminic for Local Use, U.S. Armed Forces M.J. 2:187 (Feb.) 1951.
2. Lawless, T. K.: Personal Communication.
3. Kile, R. L.: Personal Communication.
4. Levine, B.: Personal Communication.

THE TARBONIS COMPANY

4300 Euclid Avenue • Cleveland 3, Ohio



[3]In a recent study, conducted in the proctologic division of an outstanding clinic, Histar in a series of 150 patients was shown to be 25 per cent more effective than procaine in the relief of pruritus ani. (Name on request.)

THE TARBONIS CO., 4300 Euclid Ave., Cleveland 3, Ohio

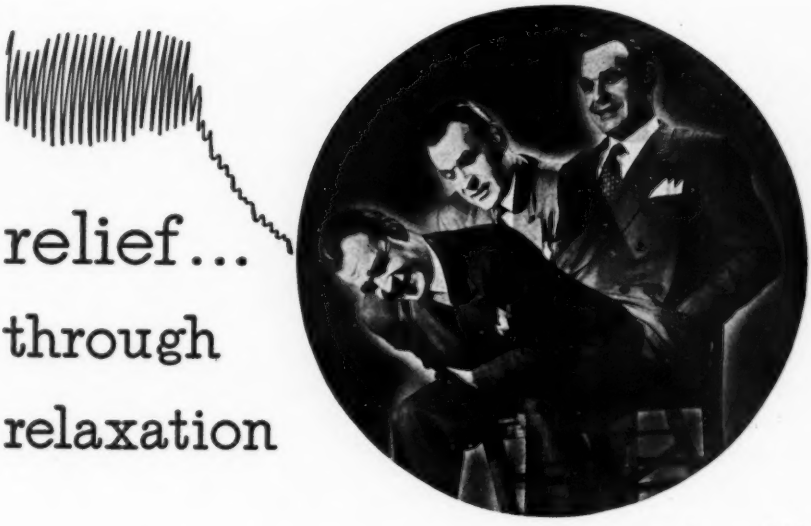
You may send me literature and sample of Histar.

_____ M.D.

Address _____

City _____ Zone ____ State _____

NYSJM 525



relief...
through
relaxation

"The most important obvious contribution of Trocinate in these ulcer patients was the relief of pain, which persisted without Trocinate, and which was only relieved when an effective dosage of Trocinate was administered."*

TROCINATE® - PHENOBARBITAL

POTENT SYNTHETIC ANTISPASMODIC COMBINED WITH A MILD SEDATIVE

- Atropine-like in its neurotropic action
- Papaverine-like in its musculotropic action
- Non-narcotic, non-toxic, virtually free of side-effects

INDICATED for the relief of smooth muscle spasm in the gastrointestinal and biliary tracts.

In a wide variety of gastrointestinal complaints, including peptic ulcer, pylorospasm, spastic colitis, biliary dyskinesia, Trocinate has been reported to be a highly effective antispasmodic, free of side-effects.

SUPPLIED as red tablets containing 65 mg. Trocinate and 15 mg. phenobarbital, and as pink tablets containing 100 mg. Trocinate; in bottles of 40 and 250 tablets.

DOSAGE 2 tablets, three or four times a day for first week; then reduce to 1 tablet, three or four times a day.

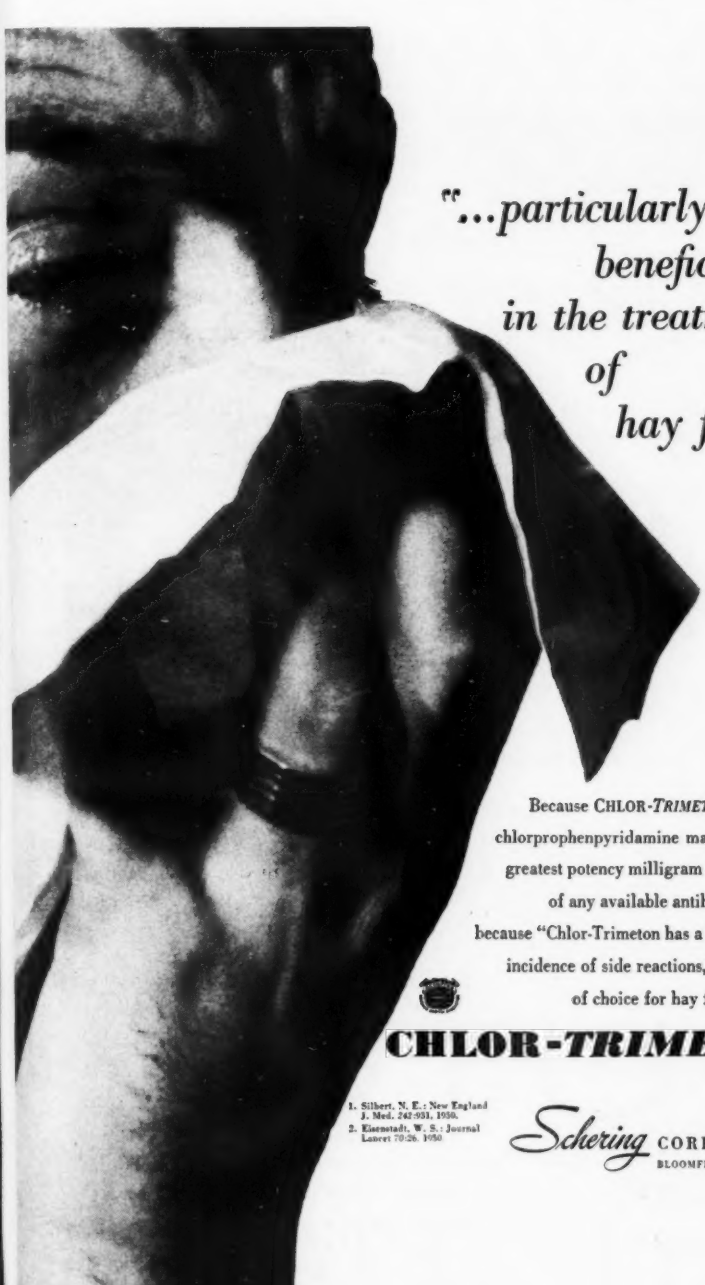
*Crawley, G. A.: *Clinical Study of Trocinate, A New Antispasmodic Drug*, M. Rec. & Ann. 43:1104, 1949.

POYTHRESS

Write for samples, reprints and literature.

WM. P. POYTHRESS & CO., INC., RICHMOND, VA.

®Reg. Trademark of β-diethylaminoethyldiphenylthioacetate.



"...particularly beneficial in the treatment of hay fever."[1]

Because CHLOR-*TRIMETON*® maleate, chlorprophenpyridamine maleate, has the greatest potency milligram for milligram of any available antihistamine, and because "Chlor-Trimeton has a relatively low incidence of side reactions,"[2] it is a drug of choice for hay fever patients.

CHLOR-*TRIMETON*
maleate

1. Silbert, N. E.: New England J. Med. 242:931, 1950.
2. Eisenstadt, W. S.: Journal Lancet 70:26, 1950

Schering CORPORATION
BLOOMFIELD, NEW JERSEY

CHLOR-TRIMETON

through i-n-t-e-r-r-u-p-t-e-d RUTOL therapy

Goodman and Gilman* stress the importance of assuring continuous response to nitrite medication by: (1) "Employing the smallest effective dose to initiate therapy, so that . . ." (2) "the dosage may be increased as tolerance develops" and (3) "cessation of administration of nitrites for several days" to reestablish "the original degree of susceptibility . . ."

RUTOL

Suggested Rx Cyclic Regimen

1 One Rutol Tablet after each meal and at night, for 2 weeks.

2 Two Rutol Tablets q.i.d., for 1 week.

3 Use alternate medication for two weeks, returning to Rutol as before.

(Pitman-Moore Brand of Rutin, Phenobarbital and Mannitol Hexanitrate)

—combines mannitol hexanitrate in suggested small dosage, 16 mg. (¼ gr.); phenobarbital, 8 mg. (⅛ gr.)—sufficient to be effective without danger of over-sedation; rutin, 10 mg. (⅙ gr. approx.) to help safeguard against capillary fragility.

PITMAN-MOORE COMPANY
Pharmaceutical and Biological Chemists
Division of Allied Laboratories, Inc.
Indianapolis 6, Indiana

*Goodman, L., and Gilman, A.: *The Pharmacological Basis of Therapeutics*, New York, The Macmillan Co., 1941.

Seven-Course "Meal" for Red Blood Cells

EXTRINSIC FACTOR INTRINSIC FACTOR

LIVER EXTRACT STOMACH TISSUE

IRON

VITAMIN B_{12} FOLIC ACID

with ascorbic acid and B complex factors

ELI LILLY AND COMPANY • INDIANAPOLIS 6, INDIANA, U. S. A.

Contains the 7 Known Antianemia Principles

PULVULES

Reticulex

(LIVER, B_{12}, IRON, AND VITAMINS, LILLY)

DOSAGE: millionths of a gram

RESPONSE: millions of red blood cells

RUBRAMIN B_{12}

Rubramin supplies vitamin B_{12}, the most potent anti-anemia substance known, in potencies to meet every need:

15 MICROGRAMS PER CC......1 cc. ampuls

30 MICROGRAMS PER CC......1 cc. ampuls
5 cc. vials
10 cc. vials

50 MICROGRAMS PER CC......10 cc. vials

Rubramin is aqueous, protein and pyrogen free, practically painless on injection, safe even for patients allergic to parenteral liver, rigidly standardized in vitamin B_{12} activity.

Also available: Solution Rubramin Crystalline (Squibb Crystalline Vitamin B_{12} Solution) in 1 cc. ampuls, 15 micrograms of crystalline vitamin B_{12} per ampul, and 10 cc. vials, 30 micrograms of crystalline vitamin B_{12} per cc.

SQUIBB

"RUBRAMIN" (REG. U. S. PAT. OFF.) IS A TRADEMARK OF E. R. SQUIBB & SONS

Above—Polydactylism, feet; upper right—Polydactylism, hand; lower right—Fungus Infection, hands.

Review them... before you show them

There are two sides to successful Kodaslide presentations. How you show your cases is important ... also what you show. That's why so many physicians and surgeons have a Kodaslide Table Viewer handy . . . use it constantly to edit their slides as well as to show them to patients and colleagues.

Review them... quickly, inexpensively with the Kodaslide Table Viewer 4X

Both a projector and a screen, the "4X" has an efficient optical system. Kodak Day-View Screen brings out full brilliance of transparencies in a normally lighted room with the projected image enlarged more than four times. Convenient slide changing. Handy focusing knob. AC or DC, 100 to 125 volts. List price, subject to change without notice, $49.50.

For further information see your Kodak photographic dealer or write:

EASTMAN KODAK COMPANY
Medical Division, Rochester 4, N. Y.

Complete line of Kodak Photographic Products for the Medical Profession includes: cameras and projectors—still- and motion-picture; film—full color and black-and-white (including infrared); papers; processing chemicals; microfilming equipment and microfilm.

Serving medical progress through Photography and Radiography

Kodak

Bromsulphalein Sodium

BROMSULPHALEIN SODIUM SOLUTION* is used as a test of liver function, especially in suspected cases of cirrhosis, malignancy, hepatitis, obstructive and arsenical jaundice. Normally the dye is removed rapidly from the blood stream by the liver, but in the presence of hepatic disease it is eliminated more slowly. The test is performed by injecting intravenously a test dose, after which the amount of dye retained in the blood is estimated colorimetrically by withdrawing a specimen of blood for comparison with a set of standards.

BROMSULPHALEIN SODIUM is supplied in 3 cc. size ampules containing a 5% sterile aqueous solution, packaged in boxes of 10. Colorimeter standards prepared from permanent dyes are also available.

Complete literature on request.

**H. W. & D. Brand of Sulfobromophthalein-sodium, U. S. P.*

HYNSON, WESTCOTT & DUNNING, INC.
BALTIMORE 1, MARYLAND
H W D

SOUTHERN MEDICAL JOURNAL

JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

PUBLISHED MONTHLY BY THE SOUTHERN MEDICAL ASSOCIATION AT BIRMINGHAM, ALA.

Volume 45 JUNE 1952 Number 6

CHRONIC PERFORATING CARCINOMA OF THE COLON*

By CLYDE A. STEVENSON, M.D.†

and

ARNO W. SOMMER, M.D.‡

Temple, Texas

Five hundred consecutive cases of carcinoma of the colon seen at Scott and White Clinic were chosen for study in an effort to determine the role of the roentgenologic examination in the diagnosis of chronic perforation. In 80, or 16 per cent of the cases, mention of perforation was made by the roentgenologist, surgeon or pathologist. Of the 80 cases, 28 were not suitable for complete study because of incomplete operation, lack of adequate pathologic specimen, or no operation. The remaining 52 cases, or 10 per cent, were studied in an attempt to determine the accuracy of a roentgenologic diagnosis of chronic perforating carcinoma of the colon and to determine the roentgenologic criteria for such a diagnosis.

The few cases of acute perforation are not included in this series but only those in which there was surgical or pathological proof of chronic gross perforation.

The roentgenologic criteria for the diagnosis of a carcinoma of the colon are a tumefactive process arising from the mucosa and projecting into the lumen of the bowel or an annular infiltrative defect which destroys the mucosa and alters the bowel wall for a relatively short distance cephalad and caudad. As a general rule the bulky polypoid lesions are in the right half of the colon while the annular carcinomas are in the left half.

When gross perforation occurs, it does so gradually and will give roentgenologic findings at variance with those of a typical nonperforated carcinoma. The absolute criteria for the roentgenologic diagnosis of a perforated carcinoma of the colon are a typical carcinomatous defect plus free gas in the abdomen, a fistulous tract or a fistulous communication with some adjacent organ (*Figs. 1, 2* and *3*).

The indirect signs of chronic perforation are a carcinomatous defect plus a longer than usual deformity, a palpable mass adjacent to the carcinoma, or fixation of the bowel at the site of the carcinoma.

It is difficult to separate by palpation the mass of the carcinoma itself and the extrinsic mass. At times the area in question cannot be palpated adequately due to its location or because of a rigid abdominal wall or marked obesity. Fixation of a carcinomatous defect is obviously not a reliable sign for several areas of the colon cannot be moved by palpation even when no disease is present. This leaves as the only fairly reliable sign the unusual length of the defect.

The accuracy of a roentgenologic diagnosis of chronic perforating carcinoma of the colon is unquestioned when a carcinomatous defect plus free abdominal gas or fistulous tract or communication is demonstrated. Sixteen of the 80 cases, or 20 per cent, showed a fistulous extension from a carcinomatous defect. Half of the extensions were into the small bowel while the others were to the bladder, uterus and stomach.

Forty pathologic specimens in which there was a chronic perforating carcinoma without fistulous communications were studied and correlated with the roentgenologic findings. The outstanding pathologic finding was, of course, a mass outside the plane of the bowel wall (*Figs. 4* and *5*).

The mass connected directly with the carcinoma and in only 9, or 22 per cent, of the 40 specimens did it fail to extend cephalad or

---

*Read in Section on Radiology, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

*From Department of Radiology, Scott and White Clinic, Temple, Texas.

†Professor of Radiology, University of Texas Post Graduate School, Temple Division, Temple, Texas.

‡Assistant Professor of Radiology, University of Texas Post Graduate School, Temple Division, Temple, Texas.

caudad outside the normal bowel wall. It is this extension which causes extrinsic pressure on the bowel and lengthens the roentgenologic defect.

FIG. 1

Small annular carcinoma just distal to the hepatic flexure. Perforation has taken place at the distal end of the lesion and there is a fistulous communication with the ileum.

FIG. 2

Large pocket formed by perforation. The carcinoma is proximal to the extrinsic extension and distal to the pocket is an area of narrowing due to the extrinsic mass.

One hundred non-perforated carcinomas were measured for length directly from the roentgenograms and the average was found to be 3.86 cm. Of the 52 cases available for complete study the average length of the roentgenologic defect was 7.5 cm. In the nine cases where the mass extended directly out into the mesentery and not up or down the bowel wall the length of the roentgenologic defect was 6 cm. or less while in all the others the defect was longer and up to 10 cm. in the sigmoid and 16 cm. in the transverse colon. Six cm. seemed to be the approximate dividing point. Lesions showing

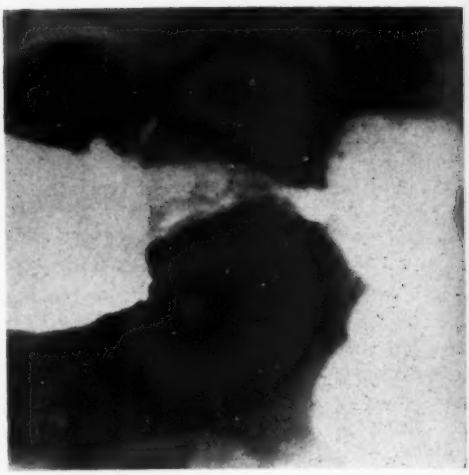


FIG. 3

Typical carcinoma of the sigmoid colon but a small fistulous tract indicates chronic perforation.

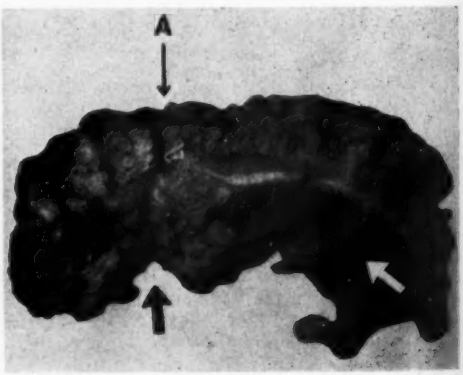


FIG. 4

Black arrow points to direct extension of a carcinoma of the colon. The white arrow indicates a large inflammatory mass outside the bowel wall. The junction of carcinoma and normal mucosa is indicated by A. Note how the inflammatory mass can compress the normal bowel.

the characteristics of carcinoma and being more than 6 cm. in length usually showed some extrinsic pressure at their proximal or distal ends.

The gross composition of this extension and extrinsic mass was of interest to us and we found that of the 52 cases the mass was made up of practically all carcinomatous tissue in 25 or 48 per cent, all inflammatory reaction in 15 or 28 per cent, and about half carcinoma and half inflammatory reaction in 12 or 23 per cent.

The roentgenologic defect caused by a nonperforated carcinoma of the colon is characterized by an abrupt change from normal bowel mucosa and wall to abnormal. This abnormal change is usually for a distance of 6 cm. or less and then it abruptly changes to normal again. Proximal to the involved area the normal colon attempts to intussuscept over the carcinomatous tissue and gives rise to slightly concave spur-like areas at the junction of normal and abnormal. This

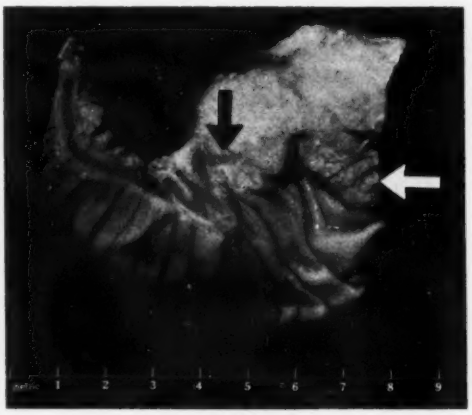


FIG. 5

White arrow indicates a polypoid carcinoma of the colon. Large mass above this is direct extension of the carcinoma. Note how this mass overrides the normal bowel (black arrow).

FIG. 6

Typical short annular carcinoma in the descending colon. No evidence of perforation.

FIG. 7

Typical short annular carcinoma in the descending colon. Double contrast roentgenogram shows the attempts at intussusception both proximally and distally, the crescentic spurs and the short irregular canal of the actual carcinoma.

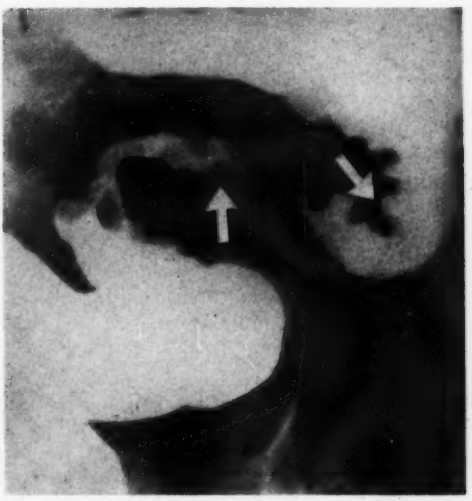


FIG. 8

Typical carcinoma of the sigmoid between the black and white arrows. Added defect between white arrows is due to pressure of the extrinsic mass on normal colon.

same appearance may be noted at the distal end of the lesion as the firm carcinomatous area attempts to intussuscept into the normal bowel (*Figs. 6* and *7*). In the presence of chronic perforation and the extension of the mass up or down the outside of the colon, these spur-like areas may be obliterated at either end of the lesion and the change from carcinoma defect to normal bowel outline is gradual (*Figs. 8* and *9*). The change from carcinomatous mucosa to normal, however, is not altered by this extrinsic pressure (*Figs. 10* and *11*).

The extrinsic pressure defect was proximal or distal to the carcinoma defect in most instances (*Fig. 12*).

This pressure defect is responsible for difficulty in differential diagnosis between a perforated

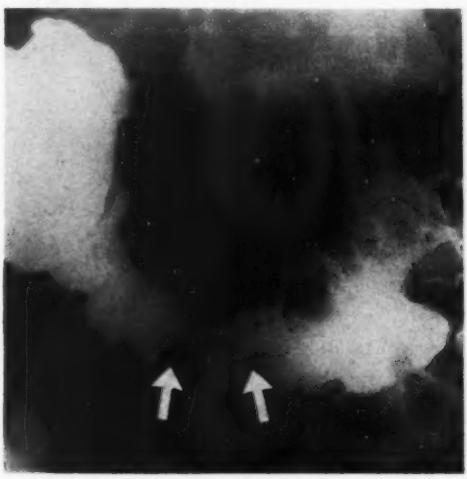


FIG. 9

Small carcinoma in the transverse colon. Perforation has caused a large extrinsic mass which compresses the normal colon both proximal and distal to the neoplasm.

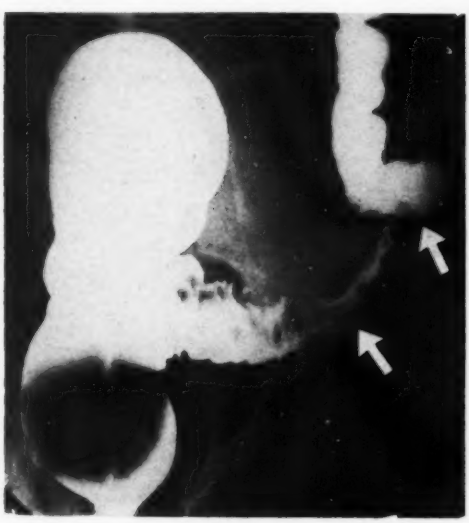


FIG. 10

Carcinoma between the white arrows. Intact mucosa and extrinsic narrowing distal to the neoplasm.

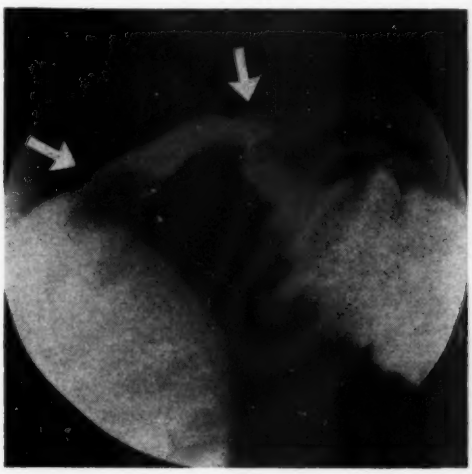


FIG. 11

Annular carcinoma between the white arrows. Note the intact mucosa in the narrowed proximal defect.

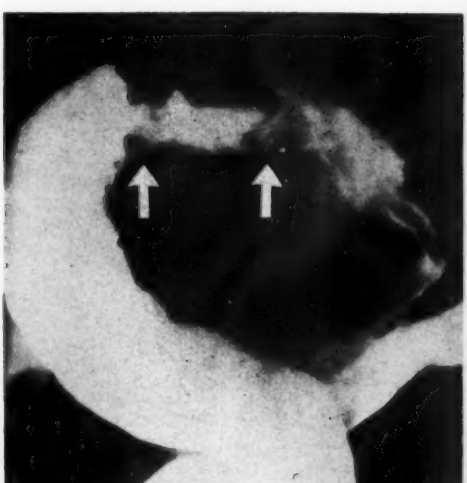


FIG. 12

Typical carcinoma of the sigmoid between white arrows. Note long area of narrowing proximal to the carcinoma. The mucosa is intact and the proximal narrowing is due to extrinsic pressure caused by the perforation.

carcinoma and segmental ulcerative disease of the colon, especially hyperplastic tuberculosis, amebiasis and idiopathic granulomas. The diagnosis of segmental ulcerative disease is based primarily on the ability to find no evidence of a carcinoma in a rather long defect. Signs favoring a granulomatous process are the absence of spurs on either end of the roentgenologic defect and the failure to demonstrate a short, irregular channel with adjacent normal mucosa even though the bowel wall is deformed by extrinsic pressure.

CONCLUSIONS

(1) From 10 to 16 per cent of this series of 500 cases of carcinoma of the colon showed gross evidence of perforation.

(2) Of the 80 cases showing some sign of perforation, 20 per cent did so by the presence of a fistula from the carcinoma to some adjacent organ.

(3) In 22 per cent of chronic perforating carcinomas without fistula formation the extrinsic mass did not compress the bowel wall and hence the roentgenologic diagnosis was not accurate in regard to perforation.

(4) The average roentgenographic length of a non-perforated carcinoma was 3.86 cm. while in 52 cases of chronic perforation the length of the entire roentgenographic defect averaged 7.5 cm.

(5) The roentgenologic diagnosis of chronic perforation adds to the gravity of the prognosis for the extrinsic mass contains gross carcinoma in about 75 per cent of the cases.

(6) Segmental ulcerative disease or a granulomatous process are differentiated from a chronically perforated carcinoma by failure to find any of the signs of a carcinoma.

DISCUSSION (*Abstract*)

Dr. Glenn D. Carlson, Dallas, Tex.—The roentgen examination of a colon constitutes a serious diagnostic challenge. Dr. Stevenson has ably brought to our attention in a variety of case reports a type of lesion which, though somewhat rare, may well be considered in our differential diagnosis. A slowly perforating neoplasm might well be overlooked in the roentgen study and might, for example, be considered diverticulitis with a minute site of perforation. Barium-filled diverticula in the adjacent bowel segments, of course, are helpful.

It is hoped that all of us will bear in mind perforating neoplasms of the large bowel.

FACTORS INFLUENCING THE PROGNOSIS OF CANCER OF THE COLON*

By RALEIGH R. WHITE, M.D., F.A.C.S.†
Temple, Texas

There are few chapters in surgery so exciting as those tracing the progress of treatment of carcinoma of the colon.[1,2] Indeed, in the last ten years developments have taken place which may outshine previous decades of endeavor. The safety of colon surgery has been so enhanced by the marked reduction in mortality and morbidity rates, that the risk of colon resection *per se* may be approaching the perhaps irreducible minimum of other major abdominal surgery of similar magnitude.[3] This is a marked contrast to the experience of ten years ago.[4,5] Notwithstanding these tremendous developments, of which we are justly proud, the test of time is the yardstick of progress in the treatment of malignant disease. The number of patients who survive five years after the resection of colon carcinoma represents, in the final analysis, what we, as surgeons, actually accomplish for the patient from a curative standpoint. That progress has been made in increasing numbers of five-year survivals is shown by the fact that the five-year survival rate after resection of colon carcinoma was only 51.6 per cent for the years prior to 1930 at the Scott and White Clinic, whereas the rate improved to 63.9 per cent for those patients resected since 1940 at the same institution. Even though some improvements have been accomplished in increasing the rate of five-year survivals, in no sense has the improvement been commensurate with the tremendous technical progress in the reduction of mortality and morbidity which has made colon surgery safer and easier for the patient. It is, therefore, of prime importance continually to check the records of five-year survivals of colon cancer, and to ascertain, if possible, the ways and means that the record may be improved.

In an effort to throw some additional light on the problem, the records were reviewed of a consecutive series of 241 patients who had under-

---

*Read in Section on Proctology, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

*From the Department of Surgery, Scott and White Clinic, Temple, Texas.

†Associate Professor of Surgery, University of Texas Post-Graduate School, Temple Division, Temple, Texas.

gone resection of the large bowel for carcinoma with the hope of cure by surgery prior to 1943. Palliative resections in patients with extensive liver metastasis or carcinomatosis were not included. These resected carcinomas could all be classed as major malignancies, for malignant polyps were purposely omitted from the review. The postoperative mortality in these 241 resected lesions was 9.5 per cent. It must be borne in mind that the majority of these patients was treated prior to the advent of the antibiotics and sulfa drugs. The mortality rate for all resected lesions of the colon was 2.5 per cent for the last three years at the Scott and White Clinic, and serves to emphasize the vast improvements in the last decade.

A minimum followup of five years was obtained fortunately on 99.1 per cent of these patients. Of the followed patients, who survived postoperatively, 60.8 per cent of patients with cancer of the colon and rectum in this series survived five years or more after surgical resection of the lesion. If postoperative deaths are included, the five-year survival rate was 55.2 per cent. The remainder of the study is based on the total number of resected cases, which includes postoperative deaths. An analysis of these cases suggests certain points worthy of discussion, particularly in regard to differences between those patients who survived five years after bowel resection and those who did not.

It is a well-known fact that the rate of cure of cancer is related to early diagnosis in the chronological age of the lesion, and in the foreseeable future, the long survival rates probably will be increased more by earlier recognition of cancer and therefore earlier definitive treatment, than by any other practical means. The average duration of symptoms before surgery in the group of five-year survivals was 10.2 months, while those patients who died in the five years after resection had prior symptoms for 11.9 months. There is no significant difference between the two groups which indicates that the duration of symptoms is not necessarily related to the chronological age of the cancer, due no doubt to the multiplicity of causes, both benign and malignant, of pain, constipation, diarrhea and melena. This serves to emphasize that cancer of the large bowel is a slow growing disease, which usually gives ample warning of its presence while it is in a curative stage, but that even though these early signs are ignored by the patient or are unrecognized by the doctor, cure may be achieved by radical surgery in over half the cases with an average duration of symptoms exceeding 10 months.

The size alone of the cancer resected apparently has little influence on prognosis, as the average recorded measurement was 5.5 cm. in the five-year survivals, and 5.6 cm. in those that did not live five years. It is well known that small carcinomas of the bowel may be associated with widespread nodal metastasis or liver involvement, while the surgeon may be pleasantly surprised to find large lesions which are apparently still localized and resectable.

Of more importance in prognosis are the grade and extent of the lesion. *Table 1* illustrates that by Broder's classification, the extremes of grade 1 cancer and grade 4 cancer are relatively uncommon in this series, (polyps removed by local excision are not included in this study), while grade 2 and grade 3 cancers comprise 94 per cent of the total graded lesions. A patient with a grade 1 resectable lesion had an 81.8 per cent chance of surviving five years; if the lesion was grade 2, the rate was 61.9 per cent, but if grade 3, the rate dropped to 44.5 per cent.

Of the greatest importance in determining prognosis, as well as resectability, is the extent of the lesion. As illustrated in *Table 2*, it is noted that 9.6 per cent of the cancers were still confined to the mucosa and submucosa, 17.3 per cent had invaded the muscularis, 46.5 per cent had in addition, penetrated the entire thickness of the bowel wall but not beyond, and 26.6 per cent of the entire group showed microscopic proof of glandular metastasis. The complete thickness of the colon was penetrated in 72.8 per cent of the total series. If the lesion was still confined to the mucosa and submucosa, 65.2 per cent lived five years. If the muscle only was invaded, 75.6 per cent lived five years. However,

GRADE OF LESION BY BRODERS' CLASSIFICATION WITH THE PERCENTAGE OF FIVE-YEAR SURVIVALS IN EACH GROUP

Broders' Classifications	Cases	Five-Year Survivals Per Cent
Grade 1	11	81.8
Grade 2	118	61.9
Grade 3	101	44.5
Grade 4	3	2 patients
	233	

TABLE 1

if the entire wall of the bowel was involved without further extrinsic spread, the five-year survivals dropped to 58.1 per cent. This report serves to confirm impressions gained from earlier studies that lymph node spread remains the most important factor in determining prognosis. If the patient had large bowel cancer involving the lymph nodes only 32.2 per cent lived five years, whereas if the cancer had not invaded regional lymphatics, the five-year survival rate rose to 63.1 per cent.

There has long been a general clinical impression that cancer of the large bowel in the patient below 40 years of age may carry a poor prognosis. It is encouraging to note that 29 patients were below age 40, and the five-year survival rate was 55.1 per cent which is similar to the rate of the entire series. Six patients were in their twenties and half of these survived five years. Glandular metastasis may indicate the same prognosis in both the young and the old, as 27.2 per cent of patients below 40 years of age with positive lymph nodes lived five years. (The five-year survival rate of all patients with positive lymph nodes was 32.3 per cent). The results of this study would suggest, therefore, that the age of the patient *per se* with cancer of the large bowel, has little influence on five-year survival rates. This does not preclude the possibility that glandular metastasis may occur earlier in the life of the cancer in the younger age groups.

Adenocarcinoma of the colon which obstructs the bowel is of serious import. The study reveals that of the resected lesions, 36 patients presented themselves to the clinic initially with signs of intestinal obstruction, grade I to IV according to the clinical severity of the obstruction. All patients had resection of the lesions after preliminary decompression, with three deaths or a mortality rate of 8.4 per cent. The five-year survival rate in patients with obstruction was 47.2 per cent, being somewhat lower but still within the range of the five-year survival rate (55.2 per cent) of the entire study. It is worthy of emphasis to note that although the patient presents himself with such a serious complication as obstruction of the colon, if preliminary decompression is done or a multiple-staged procedure is utilized and the patient is restored to physiologic balance, then subsequent bowel resection can be performed without increased mortality or greatly decreased prognosis for five-year survival.

A SUMMARY OF THE PATHOLOGIST'S REPORT OF THE AMOUNT OF PENETRATION OF THE BOWEL AND GLAND INVOLVEMENT OF THE CANCER WITH THE PERCENTAGE OF FIVE-YEAR SURVIVALS IN EACH GROUP

Involvement	Cases	Percentage	Five-Year Survivals Per Cent
Mucosa and submucosa	23	9.6	65.2
Muscle	41	17.3	75.6
Serosa	110	46.5	58.1
Glands	62	26.6	32.2
	236	100.0	
Negative glands	174	73.4	63.1

TABLE 2

Concerning the effects of irradiation upon the prognosis of carcinoma of the colon and rectum, it is difficult to draw conclusions as the early cases in the series were not standardized as to methods of treatment, due to the changing concepts of irradiation therapy during this twenty-five year period. Of the 98 cases which received x-ray or radium treatment in conjunction with definitive surgical excision of the lesion, the five-year survival rate was no better than that of the entire group.

The nature of the operative procedure is of paramount importance in the cure of cancer of the colon and rectum. Of the 241 cases resected, 27.8 per cent had a one-staged resection of the bowel with a mortality rate of 13.4 per cent. The remainder of the patients (72.2 per cent) had a multiple-staged procedure with a mortality rate of 8.1 per cent. It should be recalled that these patients were all operated upon prior to August, 1943, and that the newer antibiotics and sulfa drugs were not used in the great majority of the cases. The preponderance of multiple-staged procedures was in keeping with surgical concepts of that day which were substantiated by the lower mortality and increased protection to the patient. At the present time at the clinic, we reserve multiple-staged procedures only for the patient with obstruction, perforation or significant inflammation.

The five-year survivals and mortality rates are broken down according to the location of the cancer in the bowel as illustrated in *Table 3*. It is apparent at once that 47.4 per cent of the cancers were diagnosable at an early stage by digital examination and over half were probably evident to sigmoidoscopic study. It is worthy of emphasis that digital examination of the lower

bowel remains the most important and, in view of its simplicity, the most neglected method of diagnosis of cancer of the colon and rectum. It is evident that the mortality rates are the highest and the five-year survival rates among the lowest in cancer of the hepatic and splenic flexures. The delay of early diagnosis in these flexures due to errors in physical and x-ray examinations caused by rotation of the bowel under the overhanging thoracic cage, is well recognized. Survival rates in the descending colon are poor, also. However, it is our impression that the surgeon is apt to carry out a restricted resection in these regions, due to the difficulties of maintaining adequate blood supply to viable bowel. In the radical excision of the rectum, the blood supply is of importance only to the proximal colostomy, and here we see a creditable five-year survival rate and a reasonably low mortality. In our opinion, the surgeon should first endeavor to remove all malignant tissue with a wide protective resection of lymph bearing areas, regardless of the vascular pattern to the bowel. After the cancer is excised, is the time to locate viable bowel for anastomosis or colostomy. In hepatic flexure lesions, the ascending colon should be often included in the resection, with removal of the transverse colon should it be necessary to sacrifice the mid-colic artery with anastomosis of the terminal ileum to the descending colon. In the radical removal of a splenic flexure lesion, the mid-colic and left colic arteries may be divided, necessitating anastomosis of the sigmoid to the right colon. We have performed combined abdomino-perineal resections of the rectosigmoid with division of the inferior mesenteric artery at its origin from the aorta, including the descending colon in the resection and mobilizing the splenic flexure as a colostomy, in order to remove metastatic glands. Only by such an aggressive approach can the radical cure of cancer be extended. Exteriorization procedures of the hepatic and splenic flexures and of the descending colon, do not lend themselves as a rule to such radical measures, and this may partly account for the less favorable results obtained in these locations.

LOCATION OF 239 RESECTED CANCERS WITH OPERATIVE MORTALITY AND FIVE-YEAR SURVIVAL RATES FOR EACH GROUP

Location	Cases Per Cent	Operative Mortality Per Cent	Five-Year Survivals Per Cent
Cecum	10.8	15.3	61.1
Ascending colon	3.8	0	55.5
Hepatic flexure	4.6	36.3	45.4
Transverse colon	7.4	11.1	50.0
Splenic flexure	3.7	22.2	44.4
Descending colon	5.3	7.6	38.4
Sigmoid	17.0	14.6	60.9
Rectosigmoid	9.2	4.5	59.9
Rectum	38.2	3.3	55.5
	100.0		

TABLE 3

In conclusion, certain features of the study warrant further emphasis. It appears that the size of the lesion, the location of the cancer of the colon, the patient's statement of duration of symptoms before resection, the presence of obstruction, if the obstruction can be relieved by a staged procedure, and the age of the patient *per se*, have little influence on prognosis in this series of cases.

It is our opinion after a review of these records that the most important factors in the cure of cancer of the colon and rectum are: the early diagnosis of the neoplasm, the grade of the lesion, the extent of the cancer, and the nature of the operative procedure prompted by an aggressive and radical surgical approach.

This record is the record of the past. How may we better our results in the future? It is obvious that the grade of the lesion and the extent of the neoplasm are conditions encountered at the operating table which are not under our control. Great improvement can be hoped for, however, in earlier diagnosis and the nature of the operating procedure. The importance of early diagnosis needs no further emphasis before this body. The future may and will offer improvement, in my opinion, in the nature of the operative procedure. I have reference to the application of more radical surgery to the lesion which might have been considered inoperable in the past. Pelvic exenteration with ureterosigmoid anastomosis has a definite place in the treatment of extensive rectal carcinoma involving the bladder and other pelvic structures. I have carried out this procedure in a small group of patients who had extensive penetrating rectal malignancy without evidence of distant spread inaccessible to surgical removal. The pathology of such a case is illustrated in *Fig. 1*. There has been no mortality in this small series. All patients are alive; the first is now 18 months postoperative, has gained 40 pounds over his preoperative weight, and rides a horse every day on his ranch. Recent observation of this patient

FIG. 1

disclosed no evidence of malignant disease. The greatest immediate benefit from the operation has been the symptomatic relief experienced by these patients. Obturator nodes may be involved in these extensive malignancies. It is entirely possible that the Miles procedure for cancer of the rectum should be reinforced by pelvic lymphadenectomy as a routine procedure; especially this may be necessary in cancer involving the lower third of the rectum. In my opinion, a more aggressive approach to the problem is necessary than has been routinely practiced in the past. In this manner the rate of five-year survivals may be improved and certain "incurables" may be salvaged.

BIBLIOGRAPHY

1. Colcock, B. P.: Prognosis in Carcinoma of the Colon and Rectum. Surg., Gynec. and Obst., **85**:8, 1947.
2. Gilchrist, R. K.; and David, C. S.: A Consideration of Pathological Factors Influencing Five-Year Survival in Radical Resection of the Large Bowel and Rectum for Carcinoma. Ann. Surg., **126**:421, 1947.
3. Jones, T. E.; Robinson, J. R.; and Meade, G. B.: One Hundred and Twenty-Seven Consecutive Combined Abdomino-Perineal Resections without Mortality. Arch. Surg., **1**:109, 1948.
4. MacFee, W. F.: The Management of Carcinoma in the Several Parts of the Colon. Ann. Surg., **2**:125, 1947.
5. McKittrick, L. S.: Principles Old and New of Resection of the Colon for Carcinoma. Surg., Gynec. and Obst., **87**:15, 1948.

DISCUSSION (*Abstract*)

Dr. Raymond L. Murdoch, Oklahoma City, Okla.—We are fortunate in getting Dr. White's comprehensive review of consecutive cases excluding at one extreme palliative resections and at the other the polypectomies only microscopically malignant. The minimum follow-up of five years of 99.1 per cent of the patients, is very gratifying. As to pathology and prognosis the outstanding item seems to be that the presence of malignancy in the regional lymph nodes cuts approximately in half the chances of survival in all age groups.

Regarding location of the malignancy the survival rates are better from the peritoneal covered bowel with free mesentery. Survival is not so good in the lower half of the rectum where lateral lymphatic spread and extension gets beyond definite barriers. On the other hand a large malignancy in the original mass may do well. I have been surprised often to see this type delivered up well out of the true pelvis with five-year survivals in some young patients as well as old. The obese patient is more difficult to operate upon and has greater chance of recurrence.

In passing it should be mentioned that in 3 to 5 per cent, multiple malignancies of the large bowel occur. Malignancy develops in the earlier ages having familial multiple polyposis and not infrequently in prolonged chronic ulcerative colitis. The prognosis with these associations is bad.

There has been great improvement in operative mortality and morbidity in the last twenty years. If the public can be educated to have regular periodic proctosigmoidoscopic examinations, additional lives will be saved since three-fourths of all malignancies of the large bowel can be thus detected. A majority of them can be found by careful rectal digital examinations, but not early enough. Air contrast colon x-rays should be more generally used for the more proximal bowel, after proctosigmoidoscopic examination. No proctologist would fail to eradicate a polyp or polyps, and clinical malignancies thus would be prevented. Time is of the essence and these periodic examinations would bring to resection more cases before lymph node involvement.

BENIGN TUMORS OF THE URETER*

By W. V. PIERCE, M.D.
and
W. R. MINER, M.D.
Covington, Kentucky

Primary tumors of the ureter are among the rarest of the neoplasms of the urinary tract. Renner[1] reviewed more than 13,000 autopsies at the Vienna Pathological Institute and found only four such tumors in the group. Colston[2] could discover no more than three primary ureteral tumors in 22,000 admissions to the Brady Urological Institute, prior to 1933.

Benign tumors of the ureter are even more of a rarity than are the malignant tumors. In 1942

*Read in Section on Urology, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

Sauer[3] collected 189 cases of malignancies arising primarily in the ureter, whereas Vest,[4] in 1944, could find but seventy odd cases which had been reported as benign, and it was his opinion that perhaps only two-thirds of these could be accepted as even "probably benign." Since 1944, several additional case reports of benign ureteral tumors have been published. Even so, the total number of acceptable cases which have been reported to date remains small, possibly less than a hundred.

There are certain histological characteristics which must be present before any tumor of the ureter can be considered as benign. These include an orderly arrangement of the palisade architecture of the tumor; uniformity in the size, shape and polarity of the cells; a relative absence of mitotic figures; and complete absence of break-through or invasion of the basement membrane.

Ureteral tumors occasionally arise from the deeper elements of the wall of the ureter, but these non-epithelial types are rare. The majority of the benign tumors which have been reported were epithelial and have arisen from the mucosa or submucosa of the ureter. Three types of these have been described. First are the granulomas, which are thought to be due to chronic inflammation, and which are composed of hyperplastic mucosa or submucosa. These may accompany calculi or infection, as in the case reported by Bowen[5] in 1929. Another type is the polypoid tumor, or simple vascular polyp. These usually occur singly. They attach to the mucosa of the ureter by a narrow stalk and do not invade the deeper tissues. The vascular stroma, rather than the epithelial covering, predominates in the structure of the tumor. The third and most common type is the papilloma, which may be single or multiple, and may be sessile or villous. It is composed of transitional cells in multiple layers, with delicate connective tissue core. The majority of these tumors have been found near the lower end of the ureter.

Preoperative diagnosis of ureteral tumor is most easily made, when the tumor or a portion of it protrudes from a ureteral orifice, which has been found to occur in perhaps a third of the cases. In other instances the diagnosis may be quite difficult and the lesion may readily be missed, unless the possibility of its occurrence is kept in mind, and painstaking search for it carried out. According to Scott,[6] "tumor" was diagnosed in only 36 per cent of approximately 180 cases which he reviewed. Whenever bleeding from a ureter is encountered and there is obstruction to the passage of a catheter, together with an increase in the bleeding as the point of obstruction is probed, tumor of the ureter should be strongly suspected. Drainage of clear urine after the obstruction is passed by the catheter is further presumptive evidence that a tumor may be present.

Lich and Maurer[7] have successfully obtained tumor cells for cytological study by exerting strong suction through the tip of a catheter passed against an intra-ureteral soft tissue mass.

A filling defect in the ureterogram is the most significant x-ray finding, but is said to have been reported in only about 15 per cent of the cases.

Whenever ureteral tumor is suspected, or whenever pyelograms have failed to disclose a cause for bleeding from a ureter, serial ureterograms should be made until all portions of the ureter have been adequately visualized.

The treatment of ureteral tumors in most instances has consisted of nephro-ureterectomy. In dealing with malignant tumors, or those of suspected malignancy, there would certainly be one hundred per cent agreement among urologists as to the wisdom of this procedure, since there are few malignancies anywhere in the body which are more dangerous than those of the ureter. Even with the most radical surgery, the prognosis is often gloomy.

As concerns the treatment of benign tumors of the ureter, there are many who feel that a hard and fast rule of complete extirpation of the ureter and kidney need not apply in every instance. They believe that in certain carefully selected cases it may be possible to save the kidney by removing the tumor, with perhaps a portion of the ureter, and repairing the remaining portion of the ureter. Vest has reported three such cases, Sziberth[8] two cases, Palmer and Greene[9] one case, and Ewert[10] one case, in which conservative surgery for the removal of benign tumors of the ureter was successfully performed, with salvage of a useful kidney in each instance. There have been a few other similar reports in the literature in recent years.

Other urologists have taken vigorous exception to this form of treatment. Burns and Davis[11] have said that it should be reserved for those cases where the contralateral kidney is absent,

or is incapable of sustaining life. O'Conor[12] feels that all papillary tumors of the renal pelvis and ureter are potentially malignant, with the exception of the relatively rare simple vascular polyp. He believes that it is seldom possible to determine the degree of cellular malignancy preoperatively, and questions the accuracy of frozen sections at the operating table as a means of determining the complete absence of malignant tendencies in a tumor. In his opinion, any treatment other than complete nephro-ureterectomy with removal of a cuff of the bladder wall, is a step backward, and would tend to affect the over-all prognosis of these tumors unfavorably.

In support of those who have advocated and performed conservative surgery for selected cases of benign tumors of the ureter, the following arguments have been presented:

(1) It has been claimed that benign tumors of the ureter, whether they be Grade I papillomas, vascular polyps, or granulomas, rarely undergo malignant degeneration.

(2) There is a considerable volume of statistical evidence to indicate that Grade I tumors of the urinary tract seldom if ever metastasize.

(3) Since we do not know the basic causes which underlie the origin of many of these tumors, and since such causes may be systemic in nature, there is a possibility that after removing one kidney and ureter for a benign neoplasm, the other ureter may later become similarly affected. It has long been recognized that tumors of the bladder mucosa can arise in different areas of the bladder independently, and it seems reasonable to assume that the same could happen to the ureteral mucosa. We have heard of a case where bilateral papillomatosis of the ureters was found.

(4) If it can be correctly assumed that benign tumors of the ureter will neither metastasize nor undergo malignant degeneration, then the chief problem following the removal of such a tumor and the successful repair of the ureter would seem to be that of the possibility of recurrence or of reimplantation of the tumor. Should such occur, secondary nephro-ureterectomy would be warranted. As far as we have been able to ascertain, recurrence or reimplantation of the tumor has not been reported in any of the cases where conservative surgery for benign tumors of the ureter was employed. The follow-up periods had ranged from one to eight years, at the time the reports were submitted.

It should be emphasized that the decision to perform conservative surgery on a ureteral tumor should be reached only after the most careful study of each case, and that if there is the slightest doubt as to the benign character of the tumor, nephro-ureterectomy should be done. Preoperative x-rays may suggest that the growth is non-malignant, and thus may help in reaching the decision. No thickening or invasion of the wall of the ureter should be found at the time of the operation. Histological evidence of benign cellular structure should be obtained either from a preoperative biopsy or from a frozen section at the operative table, and confirmed as soon as possible postoperatively by study of serial sections taken through the entire operative specimen. The functional capacity of both kidneys should be known, since there would be little value in attempting to save a hydronephrotic and poorly functioning kidney, if its mate is normal.

Prolonged and regular follow-up studies of the kidney and ureter should be made in each case. Ureterograms should be made every three to six months for several years.

Since 1948 we have encountered three cases of benign tumor of the ureter in our private practice. Two of the three cases were diagnosed preoperatively as "tumor of the ureter." In one of these a diagnosis of "benign tumor" was made prior to operation, and confirmed at the time of surgery. In this last case treatment consisted of simple excision of the tumor without sacrifice of the kidney and without segmental resection of a portion of the ureter. This kidney and ureter have just been restudied almost a year and a half following surgery, and there is no indication of recurrence, implantation or metastasis.

The following case reports are given:

Case 1.—This was an 18-year-old college student. Since he was 7 years of age he had suffered recurrent attacks of aching pain in the left flank and back, often severe and incapacitating. He was cystoscoped at the age of 7, at which time a mild left hydronephrosis was found, apparently secondary to a uretero-pelvic obstruction. The kidney was functioning well, and surgery was not considered necessary at the time; but his parents were advised to have periodic check-ups performed.

In spite of the fact that there was an attack of severe pain every few months, no further x-ray or cystoscopic examinations were performed until May, 1946, when another cystoscopic examination was done because of recurrent episodes of pain, the last of which had been some two weeks previously.

Cystoscopy on May 11, 1946 revealed a left hydronephrosis with a pelvic capacity of 20 cc. There was a temporary obstruction to the passage of the catheter 22 cm. up the left ureter, which was readily overcome. Indigo carmine appeared on the left in 6 minutes in about 50 per cent concentration. The pyelogram on the right was normal, and the function of the right kidney was within normal limits. At this time, surgery on the left kidney was advised, but was refused by the patient and his parents.

On January 14, 1948, the patient was again admitted to St. Elizabeth Hospital with severe pain in the left flank and back, of 4 days' duration. The pain was very severe, and was accompanied by fever, chills and gross hematuria at the onset. There was no downward radiation of the pain, and no unusual frequency nor dysuria.

The temperature, pulse and respiration on admission to the hospital were normal. Physical examination was essentially negative except for moderate tenderness in the left costovertebral angle. Urinalysis on admission was as follows: amber; specific gravity 1.024; pH 6.0; albumin 0; sugar 0; acetone 0; microscopic, occasional pus cell. The blood count showed hemoglobin 15.5 grams, red blood cells 5,400,000; white cells 7,600; differential: polymorphonuclears 65; lymphocytes 30; monocytes 1; eosinophils 2. The blood urea nitrogen was 10.9 mg. per 100 cc.

Cystoscopy was done on January 17, 1948 under local anesthesia. The right pyelogram was normal, and there was normal excretion of indigo carmine on the right. The left ureter was obstructed at about 25 cm. No skiodan® could be injected beyond the point of obstruction into the renal pelvis, and there was no appearance of indigo carmine after 30 minutes. Intravenous urograms were done two days following this. The left kidney had a delay in excretion of the dye and there was marked retention of the dye in a hydronephrotic pelvis after three hours. On January 21, 1948, the cystoscopic examination was repeated under pentothal® anesthesia. A No. 6 catheter was passed into the renal pelvis without great difficulty, and 85 cc. of clear urine were aspirated from the pelvis. Indigo carmine appeared in 4 minutes in very dilute concentration. Retrograde pyelograms on the left showed a hydronephrotic kidney, with a stricture of the ureter just below the ureteropelvic junction. The ureter below this point was moderately dilated, and there was a filling defect in the upper ureter which suggested the presence of a tumor of the ureter (*Figs. 1* and *2*). X-rays taken three hours after withdrawing the catheter showed marked retention of the dye. Cultures from both kidneys were negative, and there was no pus reported in the urine from either kidney.

On January 31, 1948, left nephro-ureterectomy was performed without difficulty. The ureter was not opened and explored during the operation. A soft tissue mass could be palpated within the lumen of the ureter about 3 cm. below the pelvis.

The kidney which was removed measured 13x5x4 cm. The renal pelvis was markedly dilated. On opening the ureter, a stricture of the ureter, just at the ureteropelvic junction, was encountered. This reduced the lumen to one-half its normal size. Arising from the margin of the stricture were four polyps, three of which measured 3 mm. in length. The largest measured 3 cm.

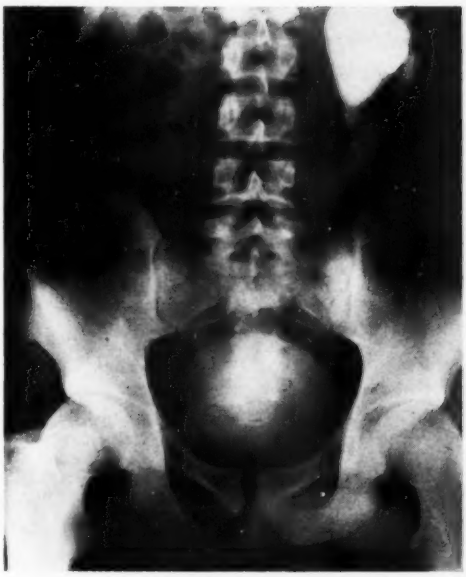


FIG. 1, CASE 1

Preoperative retrograde left pyelogram, 1948. Note filling defect in upper third of left ureter.

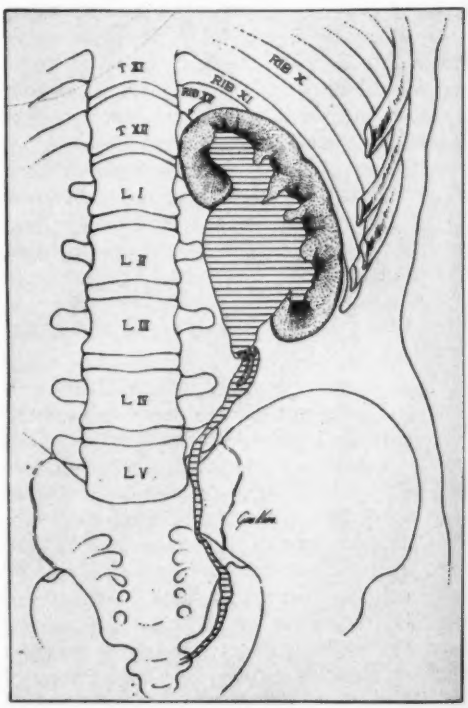


FIG. 2, CASE 1

Schematic drawing of pyelogram seen in *Fig. 4* to show relation of polyp to filling defect in ureter.

in length and 2 to 3 mm. in diameter; and extruded inferiorly through the strictured area in the upper ureter (*Fig. 3*). Microscopically, the polyps were covered by normally arranged transitional epithelium, and presented stalks of vascularized moderately cellular collagen, without significant inflammatory reaction (*Fig. 4*). The mucosa of the pelvis was essentially normal. The muscular coat of the pelvis was moderately thickened. Except for slight compression of the glomeruli and slight dilatation of the lumina of the convoluted tubules, the kidney tissue was fairly normal.

The patient had an uneventful convalescence and has had no evidence of urinary difficulties subsequently.

The ureteral tumors were diagnosed as "benign polyps of the ureter."

Case 2.—This was a 44-year-old housewife who was admitted to St. Elizabeth Hospital on April 6, 1950 because of an attack of left renal colic with chills and fever. For the previous 20 years she had suffered from intermittent attacks of sharp pain in the left flank and left costovertebral angle, each attack lasting for two or three days; and often requiring hypodermics for relief of the pain. Gross hematuria was noted with a number of these episodes. The last attack had occurred some two years previously. She had never been hospitalized with one of the attacks, and urograms had never been made prior to this illness. Her past history, except as stated above, was not relevant to the present illness. Except for these episodes of pain, she had been in good health in the past few years. Her menopause had occurred one year previously.

Physical examination on admission showed a well developed and nourished white woman who did not appear acutely ill.

Temperature, pulse and respirations were normal. The blood pressure was 118/80. There was slight tenderness in the left costovertebral angle, but neither kidney could be palpated. The examination was otherwise not remarkable. Urinalysis showed 4 to 6 pus cells and 1 to 3 blood cells per high power field. Blood count was within normal limits. The blood urea nitrogen was 9.5 mg. per cent. Intravenous urograms were made on the day following admission. The preliminary flat films of the abdomen showed a large renal calculus on the left which completely filled the lower pole calyces and a portion of the renal pelvis. Following the intravenous injection of the dye, there was a prompt excretion of

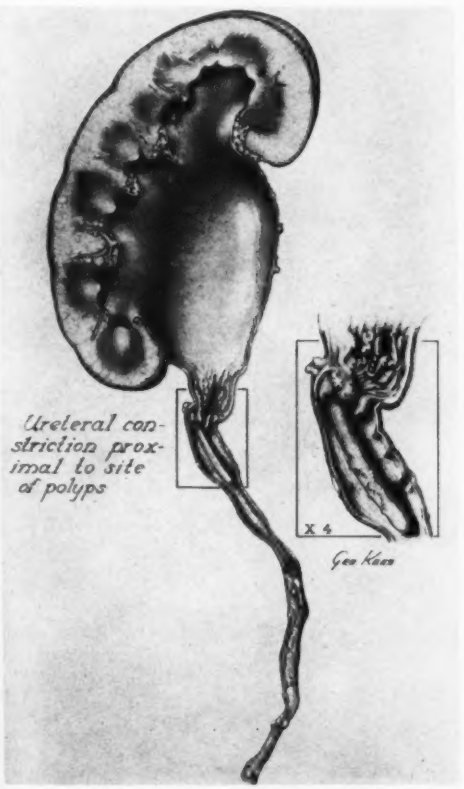


FIG. 3, CASE 1

Artist's drawing made from surgical specimen.

FIG. 4, CASE 1

Photomicrograph of polypoid tumor showing predominance of stromal tissue and absence of invasion of basal membrane.

the dye on the right, and a normal looking urogram. The dye appeared very slowly from the left kidney, but after two and a half hours the collecting system of the upper and middle pole calyces were filled. Considerable hydronephrosis was present, and there was dilatation of the upper third of the left ureter.

Retrograde pyelograms were made on the following day. The bladder was normal to cystoscopic examination. A No. 6 French catheter was passed up to each renal pelvis with ease. The urine from each side showed an occasional red blood cell and an occasional pus cell. The urine culture from each side was reported as negative. Phenolsulfonphthalein appeared on the right in 3 minutes and on the left in 8 minutes. There was 19 per cent output of the dye from the right side in the first 15 minutes, and 6 per cent in the second 15 minutes. On the left the output of dye was 5.2 per cent in the first 15 minutes, and 7 per cent in the second 15 minutes. Retrograde pyelo-ureterograms were normal on the right, but on the left revealed the renal calculus previously noted, with dilatation of the pelvis and blunting of the calyces. The ureter was dilated in its upper third (*Fig. 5*).

On April 12, 1950, left nephrectomy, with removal of the upper third of the ureter, was performed. The kidney was exposed through the usual curved left lumbar incision. On freeing the kidney it was found to be a thin walled sac. About 6 cm. below the uretero-pelvic junction there was a large blood vessel which crossed the ureter and compressed it. Since nephrectomy had been deemed advisable, no attempt was made to open the kidney or ureter prior to their removal. The ureter was ligated and divided below the vessel, and the renal pedicle was divided between ligatures of No. 3 chromic catgut. The incision was closed in the usual manner around one Penrose drain. Convalescence was uneventful, and the patient left the hospital on the twelfth postoperative day.

The pathologist's report showed the following gross and microscopic findings: the kidney weighed 165 grams, and measured 13x6x5 cm. On opening the kidney the pelvis and calyces were dilated. A large stag horn calculus measuring 4 cm. in its greatest diameter was in

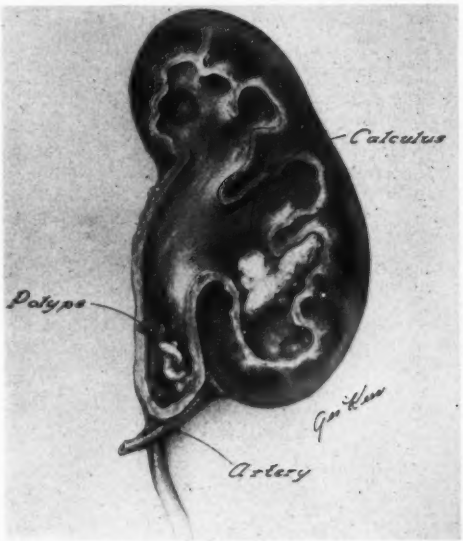


FIG. 6, CASE 2

Artist's drawing of surgical specimen.

FIG. 5, CASE 2

Preoperative left pyelo-ureterogram.

FIG. 7, CASE 2

Photograph of upper ureter showing cluster of polyps.

the pelvis and lower calyces. The mucosa of the pelvis was diffusely thickened, focally hemorrhagic and granular. Many of the calyces were diffusely hemorrhagic. The renal substance was reduced in thickness. The mucosa of the ureter was similar to that of the renal pelvis and calyces. About 4 cm. below the ureteropelvic junction there was a cluster of mucosal polyps which formed a conical structure approximately 8x5x2 mm. There were three polypoid structures, 1 approximately 8 mm. in length; the other two approximately 5 mm. in length. Just below these the lumen of the ureter narrowed down (*Figs. 6* and *7*).

On microscopic examination, multiple sections of the kidney revealed essentially normal architecture except for the fact that the thickness of the organ was considerably attenuated. The peripelvic tissues were infiltrated with a moderate number of histiocytes and a few lymphocytes. This tissue was moderately edematous. Focal erosions of the pelvic mucosa were seen. In several sections the renal architecture was distorted with fibrosis and organizing granulation tissue which was infiltrated with lymphocytes and histiocytes. The renal tissue bordering on such zones was likewise the site of chronic inflammatory reaction.

The mucosa and wall of the ureter were essentially normal except that in the region from which the polyps arose there was a diffuse lymphocytic and macrophagic inflammation in the subepithelial tissues. The polyps presented broadly vascularized collagenous stalks, infiltrated with inflammatory cells, and covered by metaplastic squamous epithelium (*Fig. 8*).

The diagnosis was: ureteral polyps, with squamous metaplasia and marked chronic inflammation; renal calculus; hydronephrosis; chronic pyelonephritis; chronic ureteritis.

Since the ureteral polyps showed no indication of invasion of the submucosa, nor other evidence of malignancy, secondary removal of the ureteral stump was not considered necessary. The patient has had no urinary complaints since the operation.

Case 3.—This 26-year-old white woman, single, was admitted to St. Elizabeth Hospital on April 24, 1950 with chief complaint of painless hematuria. She began to notice blood in her urine one week previously. The blood was present throughout urination and was fairly heavy at times. There was no associated burning nor pain, nor was there any history of chills, fever, frequency nor nocturia.

The past history was essentially negative, except that in 1944 the patient had been admitted to St. Elizabeth Hospital with right flank pain and hematuria. These symptoms had lasted for only a few hours, and intravenous urograms the following day were reported as normal. There were no urinary symptoms during the intervening six years, prior to the present illness.

FIG. 8, CASE 2

Photomicrograph of polyps showing squamous metaplasia of epithelium and predominance of stromal tissue. Note absence of invasion of basal membrane.

FIG. 9, CASE 3

Preoperative retrograde pyelo-ureterogram, right. Note filling defects in lower third of ureter.

The physical examination on admission to the hospital was essentially negative. Blood pressure was 130/80. There was no costovertebral tenderness on either side. The blood count was within normal limits. Urinalysis showed 4 pus cells per high power field, but was otherwise normal. The blood urea nitrogen was 6 mg. per 100 cc. Intravenous urograms on April 25, 1950 were normal. No calcific shadows were present on the plain film. Following the intravenous injection of the contrast medium there was prompt and good excretion of dye from both kidneys, and normal appearing pyelograms bilaterally. The ureters did not fill adequately on these films, but there was no evidence of ureterectasis or of pyelectasis.

On April 26, 1950 cystoscopic examination was done. When the cystoscope was introduced into the bladder a long polypoid tumor could be seen projecting from the right ureteral orifice into the bladder. This intravesical protrusion was about 5 cm. in length, but with each peristaltic contraction of the ureter, an additional 2 or 3 cm. of the tumor would come down into the bladder, then again retract up into the ureter as the ureter relaxed. The polyp was club shaped on the end, and tapered down to a slender stalk-like appearance proximally. Owing to the length of the tumor, it was readily grasped with forceps under cystoscopic vision, and pulled down through the urethra until about 3 cm. of the

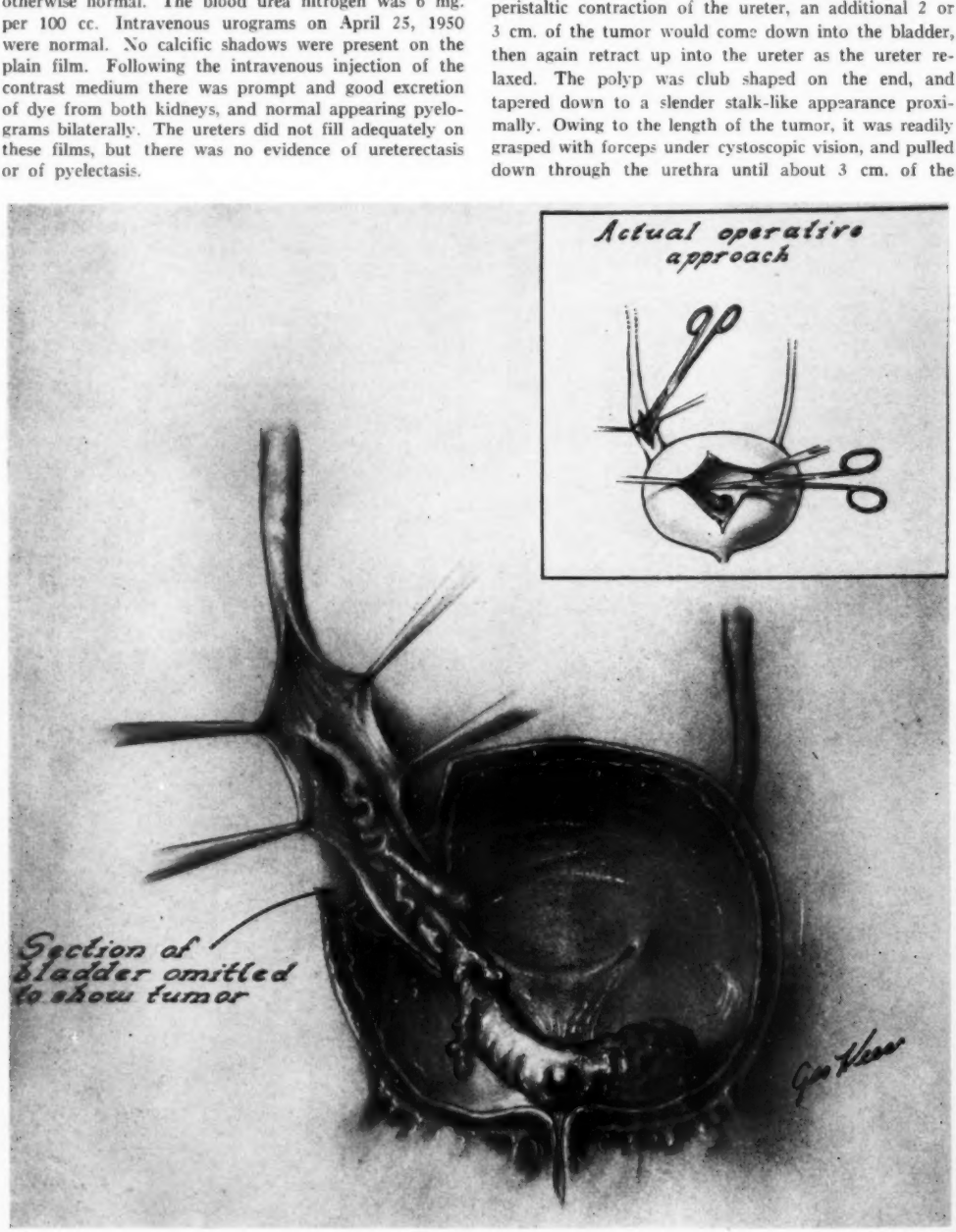


FIG. 10, CASE 3

Artist's drawing of tumor arising from mucosa of lower third of ureter and projecting into bladder. Inset shows actual operative approach.

terminal portion projected outside the urethra, where a section was excised for pathological study, before replacing the tumor within the bladder.

A No. 7 ureteral catheter was then passed up to the right renal pelvis without difficulty and retrograde pyelo-ureterograms were made. These showed no evidence of obstruction or dilatation of the ureter or renal pelvis. In the lower third of the ureter a large irregular filling defect could be seen (*Fig. 9*). The left pyelo-ureterogram was normal. Phenolsulfonphthalein output was 10 per cent on the right and 15 per cent on the left in 15 minutes. There was an occasional pus cell in the urine from either side, but cultures from both sides were reported as negative.

Pathological report on the tissue which had been removed for biopsy stated that sections of the material revealed collagenous connective tissue in which were many small blood vessels, some dilated and congested, and a marked diffuse inflammatory reaction, with focal necrosis of the collagen in some areas, and with small amorphous faintly acidophilic structures scattered sparsely through the substance. These structures were surrounded by sharp basement membranes and were suggestive of epithelium but were necrotic and could not be definitely evaluated. Epithelial substance was not found about the periphery of the masses. The diagnosis was "Marked chronic inflammation of the wall of the ureter with focal necrosis."

On May 5, 1950, the right ureter was explored through a midline subrapubic incision. The lower third of the right ureter was exposed down to the bladder. The bladder was opened, and by exerting traction on the intravesical end of the polyp, it was possible to localize the point of attachment of the tumor to the wall of the ureter. A longitudinal incision in the ureter was made over this point which was about 5 cm. above the meatus, and the base of the tumor, together with the attached ureteral mucosa, was excised (*Fig. 10*). The underlying muscular layers of the ureter were not infiltrated nor attached to the base of the tumor, and it was not considered necessary to excise any of the wall of the ureter, nor to fulgurate the ureteral wall where the base of the tumor had been attached.

A No. 10 French soft rubber catheter was passed through the bladder up the ureter to the right renal pelvis, as a ureteral splint, and the distal end of this was brought out the urethra and attached to a No. 18 Foley retention catheter. The incision in the wall of the ureter was closed over the splinting catheter with a few interrupted sutures of fine chromic catgut. The incision in the bladder was closed primarily. Soft rubber drains to the ureter and to the bladder were brought out through a stab wound, and the suprapubic incision was closed routinely.

FIG. 11, CASE 3

Photograph of the entire tumor following its removal.

FIG. 12, CASE 3

Photomicrograph of polypoid tumor. Note predominance of stromal tissue, normal adult transitional epithelial covering, and absence of invasion of basal membrane.

Convalescence was uneventful. The splinting catheter was removed in 15 days. Intravenous urograms on May 25, 1950 were normal in appearance. The patient was dismissed on the twenty-second postoperative day. She has remained entirely free of symptoms referable to the urinary tract since then. In October 1950, she was cystoscoped and retrograde pyelograms were made, which revealed no abnormalities of the kidney, bladder, or ureters. The renal function was normal bilaterally. She was advised to return for another checkup in 6 months, but did not do so until September 1951. At this time, she was cystoscoped. Both kidneys were free of infection and were functioning normally. The pyeloureterograms were entirely normal.

The pathological report on the excised polyp is as follows (*Fig. 11*): "Gross examination: The specimen is a 9.5 cm. tubular structure which varies in diameter from 2 mm. to its base to 8 mm. at its tip. The tip is reddish-brown, soft and granular. Elsewhere generally the surface is smooth and hyperemic. From one border there arise numerous small fronds varying in length up to 5 mm. and one up to 10 mm. long. These fronds arise from the basal three-fourths of the specimen, and at the base there is a small cuff of mucosa approximately 2 mm. in width."

"Microscopic examination (*Fig. 12*): Three sections were made. There is a thick edematous focally hemorrhagic collagenous stroma in which there are thin-walled dilated congested blood vessels and within this stroma there is a sparse diffuse and moderate focal lymphocytic and macrophagic reaction along with some polymorphonuclear leukocytes. From the surfaces of these sections there arise secondary projections of stroma and the entire structure and the projections are covered by a layer of adult transitional epithelium. The epithelium is everywhere sharply delineated from the stroma.

"Additional sections taken through the basal portion of the tumor showed similar changes."

The diagnosis was ureteral papilloma.

SUMMARY

Benign tumors of the ureter are being reported in the literature in increasing numbers, but they are still among the rarest of the neoplasms of the urinary tract.

Three case reports of benign tumors of the ureter are presented in this paper. Two of these were diagnosed preoperatively as "tumor of the ureter," and in one of them a correct diagnosis of "benign tumor of the ureter" was made prior to the operation.

Nephro-ureterectomy was done in one of the cases, and simple nephrectomy, with removal of the proximal portion of the ureter, in another. In the third case treatment consisted of excision of the tumor through a longitudinal incision in the wall of the ureter, together with removal of the attached portion of the ureteral mucosa. Careful x-ray studies almost a year and a half following the operation have revealed no evidence of recurrence of the tumor, or of obstruction to the ureter or kidney.

Review of the literature reveals that conservative surgery has been successfully carried out in a few other cases of benign ureteral tumors, apparently without subsequent development of metastases or recurrence.

It must be emphasized that this method of treatment should be used only in carefully selected cases, and after the most painstaking study of each case. Regular and systematic follow-up studies are essential if this treatment is to be employed.

REFERENCES

1. Renner, M. J.: Primary Malignant Tumors of the Ureter. Surg., Gyn. & Obst., **52**:793-803, 1931.
2. Colston, J. A. C.: Primary Tumors of the Ureter. Trans. Assoc. Genito-Urinary Surg., **26**:41, 1933.
3. Sauer, H. R.: Case of Large Bone Metastasis from Carcinoma of Ureter, Complicated by Congenital Giant Hydronephrosis. J. Urol., **48**:467-473, 1942.
4. Vest, S. A.: Conservative Surgery in Benign Tumors of the Ureter. J. Urol., **35**:97-121, 1945.
5. Bowen, J. A.: Obstructing Papilla of the Ureter: The Result of Infections and Calculus. New England J. Med., **200**:1091, 1929.
6. Scott, W. W.: Review of Primary Carcinoma of Ureter, Presenting Two Cases. J. Urol., **50**:45-64, 1943.
7. Lich, Robert Jr.; and Maurer, Joseph: Personal Communication.
8. Sziberth, Karl: Critical Considerations and a Contribution of the Radical Operation of Solitary Ureteral Papilloma. Urol. and Cut. Rev., **52**:383-385, 1948.
9. Palmer, James K.; and Greene, Lawrence F.: Benign Fibromucous Polyp of the Ureter. Surg., **32**:562-565, 1947.
10. Ewert, Earl E.; and Duncan, Robert J: Primary Tumors of the Ureter. Surg., Clin. N. America, **31**:623-631, 1951.
11. Burns, Edgar; and Davis, David M.: Discussions of paper by S. A. Vest. J. Urol., **35**:97-121, 1945.
12. O'Conor, Vincent J.: Treatment and Prognosis of Papillary Tumors of the Renal Pelvis and Ureter. J. Urol., **61**:488-492, 1949.

33 East Seventh Street

DISCUSSION (*Abstract*)

Dr. Hugh T. Beacham, New Orleans, La.—As indicated in Drs. Pierce and Miner's presentation, tumors of the ureter are rare, particularly benign growths. Many urologists have never encountered one. At the large Charity Hospital of Louisiana at New Orleans among the records of 27,098 patients admitted to the urologic services from July 1, 1940 to June 30, 1951 only one case of benign ureteral neoplasm was found. During these eleven years 29,305 cystoscopies were performed. At the Southern Baptist Hospital in New Orleans from 1940 to 1951, 7,117 cystoscopic examinations were made and one benign tumor of the ureter was found among the records of this institution. During the last 11 years among 4,019 urologic admissions to the Hotel Dieu, Sisters' Hospital in New Orleans no case of benign ureteral tumor was found.

Through the courtesy of Dr. Robert W. Willoughby the case at Southern Baptist Hospital is reviewed. A 22-year-old white man was admitted to the hospital

October 6, 1947 with the complaint of recurrent hematuria for 6 years. He had received antibacterial therapy on several occasions. Retrograde pyelography on September 30, 1947 had revealed a filling defect in the middle portion of the left ureter. This defect persisted on repeated visualization. A hematologic survey was normal including bleeding and coagulation times, prothrombin determination, platelet counts and fragility tests. The urine continued to reveal hematuria without pyuria. Blood chemical studies were normal. On October 15, 1947 the left kidney and upper two-thirds of the ureter were removed. The midportion of the left ureter was thickened and exhibited an angiomatous mucosal lesion. Slight hydro-ureter was noted. The kidney exhibited evidence of recurrent pyelonephritis.

The case at Charity Hospital was that of a 62-year-old white man, who was admitted April 6, 1942 with congestive heart failure. One year previously, retrograde pyelography had revealed a filling defect in the lower third of the left ureter. At this time gross hematuria had been noted. The patient refused surgical therapy. Repeated pyelography revealed persistence of the filling defect and pyuria, with Streptococcus fecalis as the principal organism. In spite of therapy the patient died in congestive failure on April 22, 1942. Autopsy revealed benign papillomata of the middle and lower thirds of the left ureter. The largest papilloma was 2 cm. in diameter with a small pedicle. Only a moderate degree of hydro-ureter was noted.

Drs. Pierce and Miner are due congratulations on their presentation of proper management of three cases and discussion of the subject. In order for us to be mindful of the rarer lesions it is necessary for such reports to be made. Proper suspicion of these tumors should lead to earlier recognition and proper therapy for more patients.

In regard to the type of surgery to be performed it would appear that since malignant primary tumors of the ureter are more common than benign tumors, one should rule out the possibility of malignancy before making a decision. This requires biopsy. A lesion protruding into the bladder is rare so usually diagnosis would necessitate exposure and excision of the ureteral lesion at the time of operation. Frozen section at this time appears indicated; however, by this method certainty as to diagnosis is limited. In regard to resection of segments of the ureter, one must be mindful of failure of healing or stricture formation. It is my opinion that when in doubt as to the diagnosis or as to the feasibility of resection, nephrectomy and ureterectomy are in order. In the majority of reported cases renal impairment has been present and this has to a large extent accounted for the high percentage of nephro-ureterectomies.

Dr. Vincent Vermooten, Dallas, Tex.—I wish to compliment the authors' photographer on producing the most excellent slides of pyelograms that I have seen projected at any urologic meeting I have attended during the past twenty-five or thirty years. I wish that his technic could be adopted as the standard to be aimed at by all urologists. For information of those who may be interested, Dr. Pierce tells me the photographer is Mr. Lewis J. O'Brien, 219 North Cooper Avenue, Cincinnati 15, Ohio.

MEDICAL USES OF COBALT 60*

By HERBERT D. KERMAN, M.D.†
Oak Ridge, Tennessee

Through years of experience and clinical usage, radium has found a definite and extremely valuable position in clinical radiotherapy. It has not been dislodged from this situation by newer roentgen ray technics and still remains the treatment of choice for certain forms and stages of malignant disease. Likewise its use, in combination with conventional x-ray therapy or with surgery, affords optimum therapy in certain neoplasms. However, established indications for the use of radium have been jeopardized by the fact that, except in relatively few centers and with few individuals, there is not an adequate supply of radium either in quantity or, more important, in variety of applicators for particular radiotherapeutic problems. The primary reason for lack of suitable supplies of radium has been its prohibitive cost. Except in the larger centers, an adequate supply of radium for all its possible uses cannot be kept on hand awaiting the proper case. As a result, only a small supply in a form suitable for the more common situations is available.

Radioactive cobalt appears to be one of the most suitable of the few radioisotopes which have been found to offer distinct possibilities as effective therapeutic agents in medicine. In 1946, Mitchell,[1] Coliez,[2] and in 1948, Myers[3] suggested that cobalt 60 in either its relatively pure form or as a suitable alloy would serve as an ideal "radium substitute."

It is my purpose to point out that cobalt 60 is not only an efficient, relatively cheap substitute for radium, but in many ways would seem to be superior to radium in its physical and radioactive properties and therefore a more suitable isotope than radium. If high flux nuclear reactor time were to be fully available, radiocobalt in any reasonable quantity, strength, or form could be obtained at moderate cost, so that any center or individual with proper training and qualifications should be able to procure this material for use in indicated situations.

*Read in Section on Radiology, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

†Medical Division, Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tennessee. On leave of absence from University of Louisville School of Medicine, Louisville, Kentucky.

Properties of Cobalt.—Cobalt is a grey-white metallic element closely related to iron and nickel. It has an atomic weight of 58.94, an atomic number of 27, a melting point of 1,480° C., and a boiling point of 3,000° C. It has a density of 8.9 and is a hard, malleable, ductile, and extremely magnetic metal. Its principal ores are usually a sulphide (cobalt glance, CoAsS) and an arsenide (smaltine, $CoAS_2$). It can be prepared by reduction of its oxides in a current of hydrogen. Its alloys and salts are very important in commercial and industrial applications. At ordinary temperatures pure cobalt, because of its hexagonal crystal structure, is very difficult to work; however, relatively pure cobalt alloys can be machined and worked without great difficulty. Pure cobalt plates or sheets can be produced easily by electroplating; and cobalt wire may be obtained in relatively pure concentrations, either by drawing or by electroplating wired nickel or brass with a heavy coating of cobalt. Myers[3] has suggested that an alloy composed of 45 per cent cobalt and 55 per cent nickel, known as "cobanic," may be suitable for use in interstitial work. Various cobalt salts which are readily soluble in ordinary solvents are easily obtainable.

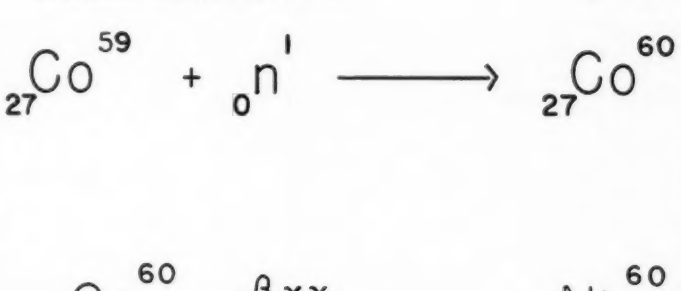


FIG. 1
Nuclear reaction for preparation of cobalt 60 in pile.

Preparation and Properties of Radioactive Cobalt.—The element cobalt occurs in nature only as cobalt 59. There are six radioactive isotopes of cobalt, with atomic weights of 56, 57, 58, and two with atomic weights of 60. In both the cyclotron and pile production of cobalt 60, isomeric radioactive nuclides with half-lives of 10.7 minutes and 5.3 years may be formed. Only a very small part of cobalt 60 produced in a nuclear reactor is the 10.7 minute isomer. This form disintegrates by isomeric transition to the long-lived isotope. The nuclear reaction in the chain-reacting pile which produces the radioactive isotope of cobalt is the common "neutron capture" followed by gamma ray emission, the so-called n-8 reaction. This may be written as shown in *Fig. 1.*

Radiocobalt 60 has been available since 1937 and has been widely used in various laboratories as a gamma-ray standard. The most accurate value of the gamma-ray energies, as described by Evans,[4] is through two metastable states with the emission of a beta ray of maximum energy of 0.308 Mev. followed by two gamma rays in cascade of 1.169 and 1.331 Mev. respectively. The disintegration scheme as given by Evans is reproduced in *Fig. 2.* Thus, cobalt 60 may be

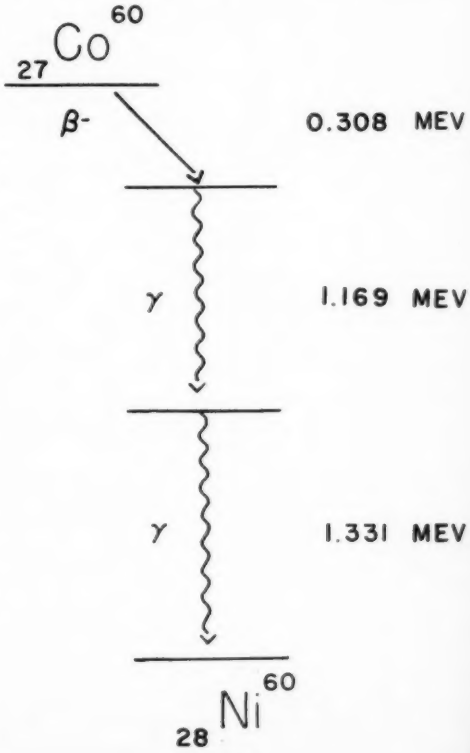


FIG. 2
Disintegration scheme of cobalt 60.

regarded as a source of monochromatic gamma rays of mean energy of 1.2 Mev.

From examination of the disintegration scheme, one sees that the gamma radiation emitted from cobalt 60 is much simpler in character than that emitted from radium sources, the latter consisting of some 20 photons. These are emitted chiefly from RaB and RaC in equilibrium with radium and extend up to 2.27 Mev. with possible feebler higher energy components.

If we examine the equivalence of energy of radium and cobalt 60, we find that one millicurie of cobalt 60 (unfiltered) gives the same dosage rate (R/min.) as 1.63 mg. of radium filtered under similar geometrical conditions. A theoretical one-millicurie point source of cobalt 60 (unfiltered) would deliver 13.5 gamma roentgens per hour at 1 cm. distance, whereas one milligram of radium with 0.5 mm. platinum filtration yields 8.4 roentgens per hour under similar geometric conditions. In terms of activity, therefore, a 100-curie source of cobalt 60 is equivalent to 163 grams of radium.[5]

In considering both the primary and secondary beta-ray emissions from radium and cobalt sources, respectively, we again find an advantage with cobalt 60.

A radium source emits beta rays of maximum energy of 3.1 Mev. from RaC and 0.65 Mev. from RaB. This energy emission is about 70 per cent of the energy emitted per hour as gamma rays.[6] The cobalt source emits electrons of low energy (maximum 0.308 Mev.), so that the average energy of beta rays emitted is only 0.1 Mev. assuming normal distribution of numbers of electrons in the momentum spectrum. For each disintegration, therefore, the Co^{60} atom emits 0.1 Mev. in energy of electrons for each 2.4 Mev. energy in gamma ray quanta. Thus the amount of energy emitted as electrons is only 5 per cent of that emitted by gamma rays, compared with the value of 70 per cent for radium.

In considering the secondary electronic emission, we again find an advantage with Co^{60}. It is well known that the minimum electronic emission resulting from the gamma rays of radium traversing various filters was produced when these filters were made of some material of intermediate atomic number.[7] Thus the secondary electronic emission from cobalt sources under the action of their own gamma rays is likely to prove much less intense than the electronic emission from heavy elements such as platinum used to screen radium sources. We can, therefore, anticipate less troublesome necrosis in the area immediately surrounding an interstitial cobalt source than with a similar radium source, because of reduction in both primary and secondary emission. In considering the shielding necessary for removal of the caustic beta ray emission, we find that the thick screens necessary with radium are appreciably reduced with radiocobalt so that the old filtration problem of radium is minimized by use of radiocobalt.

In the preparation and handling of both sources, again several advantages of radiocobalt over radium seem apparent. The complex weighing and packing procedures necessary with the powdered radium salt are avoided, as cobalt is in a form suitable for therapeutic use at the time of its insertion into the slow neutron flux of the pile. The magnetic property of cobalt lends itself very readily to a simple electromagnetic device which facilitates handling. In addition, there is no wait of a month or two to obtain radioactive equilibrium, as with radium sources.

Since radiocobalt ends its life as stable Ni^{60}, no radioactive family or chain is involved in which gaseous or inconvenient products are formed, and the old radon leakage problem disappears. Also, the linear density of the cobalt source remains constant throughout its length of life without the danger and difficulty of the shifting of radium salt which sometimes occurs within radium needles and results in poor distribution of radiation intensity. Leakage of the active salt as the result of inferior preparation or of breakage cannot occur with cobalt.

Untoward absorption of cobalt has been described by Nickson, Lamerton, and Mayneord,[8] in which measurable activities of radiocobalt have been found in the excreta of rats following implantation of cobalt wire and discs. However, as cobalt is rapidly eliminated from the body,[9] no problem of retention or storage exists, as has been described with radium. It would seem very undesirable, however, to use pure cobalt parenterally, as flaking of radioactive cobaltic oxides into tissue is to be avoided. Interstitial and intracavitary applicators, however, can be easily sheathed with monel, nylon, or stainless steel so as to avoid this possible complication.

USES OF RADIOCOBALT IN MEDICINE

The preceding description of the physical and radioactive properties of cobalt would indicate that it would be a suitable agent for interstitial, surface, intracavitary and teletherapy radiation. Now let us examine these possible modalities in medicine.

Interstitial.—J. L. Morton[10 11] and William G. Myers and associates[3] at Ohio State University have pioneered in the clinical use of interstitial cobalt and have developed precise technics in handling this material, as well as in its application in certain tumors. Morton has developed a method for individualized interstitial radiation in carcinoma of the cervix by the use of monel metal and stainless steel tubes containing radioactive cobalt wires, spacing them in desired positions with aluminum wire or graphite spacers. These sources are then implanted through lucite guides in such a fashion as to produce uniform and equal distribution of the radioactivity. This technic would seem more fully to satisfy the principle of uniform distribution of dosage than with conventional free-hand implantation methods. The needle distribution can be individualized to the patient's needs and, in addition, the individual needle strength can be regulated to provide maximum efficiency whereby precision dosage can be achieved. This method has been adapted to conform with the dosage system outlined by Paterson and Parker. Meschan[12] and associates have also described the use of radiocobalt 60 wire, sheathed by a hyperchrome steel tubing which effectively reduces the beta radiation. This tubing is readily made into needles and is resistant to body fluids. They have also prepared a standardization technic and have presented corrected Paterson-Parker charts for use with cobalt 60 sources.

Radiocobalt offers much greater flexibility and accuracy in the physical planning of treatment than is possible with fixed radium needles. It is possible to construct radiocobalt needles that are differentially loaded to give additional radiation to certain areas of tumor and to eliminate the need for "crossed ends," which is often impractical in radium needle implants. More recently Morton, Callendine and Myers[11] have been utilizing small radioactive cobalt wires, placed and spaced in a very plastic fine hollow tube, which can be utilized in areas which cannot be implanted satisfactorily with rigid needles. This flexible linear source can be made to follow the contours of the tumor infiltration, and it is possible for the therapist to sew sources into any treatment site that can be reached by a needle. This technic results in surprising uniformity of distribution of the radioactive material. These ingenious technics appear to offer many interesting possibilities and challenges to the radiotherapist.

Surface.—Radiocobalt sources may easily be used as surface applicators in the conventional manner. However, by reason of its physical and radioactive properties, radiocobalt becomes extremely versatile. With imagination, one can foresee applicators devised from cobalt foil or made by plating or spraying the material on specially constructed molds. Flexible linear sources may be devised to meet difficult anatomical situations. Scheer[13] has recently suggested the use of a plastic uniformly impregnated with Co^{60} in powder form. This plastic may be cut to desired shapes for direct application to a tumor. This use of cobalt seems to be limited only by ingenuity of the therapist.

Intracavitary.—In intracavitary radiation, particularly in malignancies involving the maxillary sinus, nasopharynx and bladder, Low-Beer[14] has described the use of beads containing metallic cobalt, which are bored and threaded and activated in the reactor to the desired strength. These beads may then be plated and calibrated against radium standards. Beads were chosen because this would more accurately approach point sources of irradiation. This point source was placed in an inflatable catheter which would hold the bead in place in a central position, so that equidistant distribution of radiation would occur on all surfaces of the cavity. Accurate dosage calculations can be made for the wall of the cavity and at various depths.

A further application of intracavitary radiocobalt which may be worthy of investigation is the use of radioactive cobalt solutions encased in thin-walled rubber containers for use in irradiation of the vagina, uterus and bladder. Likewise, development of partially shielded or compartmented catheters for adequate shielding of normal areas should be investigated. Such an application is currently under investigation at the Medical Division of the Oak Ridge Institute of Nuclear Studies.

Teletherapy.—The availability of the cobalt from nuclear reactors in very high specific activity sources makes possible teletherapy units

in the supervoltage range. The use of 5-10-gram teleradium units, particularly in this country, has slowly been abandoned in favor of supervoltage x-ray equipment. As pointed out by Grimmett[15] and Wilson,[16] the disadvantages of teleradium units is inherent in the physical characteristics of radium. In order to exploit the penetrating power of the gamma rays of radium, one must use radium at a distance of 50 cm. or more in order effectively to increase the percentage depth dose. With the quantities of radium available, the intensity of radiation reaching the patient would be too low to be biologically useful if the focal skin distances were to be increased to 50 cm. To compensate for this loss of intensity, larger quantities of radium would be necessary. Excessive cost makes this quite impractical. In addition, certain physical properties would make larger quantities of radium undesirable as a single teletherapy source. For example: because of the pressure of radon it has been generally recognized that the maximum amount of radium that can be packed into one tube is approximately 200 mg. In order to make a source of several hundred grams, the size would necessarily be so large as to produce extremely undesirable penumbra effects on the skin. The bulk of such a source would make pneumatic transfer from a storage unit to a treatment head undesirable, and would complicate any design of treatment-head and applicators. Radiocobalt, on the other hand, has none of these disadvantages. In addition to the obvious financial advantage, it is quite possible in a high flux nuclear reactor to obtain radiocobalt sources of approximately 35-50 curies per gram, so that a source as small as 2 cm. in diameter may contain 2000-3000 curies. This would bring undesirable penumbra effects, mechanical, handling, and shielding problems to a practical level.

Radiocobalt teletherapy units would compare quite favorably with existing supervoltage x-ray equipment. A telecobalt unit will yield the same energy beam (1.2 Mev.) as the effective wavelength of a 2-Mev. x-ray generator, without the soft components which exist in the x-ray spectrum. It will have either as good or better flexibility, mobility, and ease in clinical adaptation to therapy as the x-ray unit. The maintenance problems and electrical problems of high tension generation will be avoided. It will compare quite favorably with the x-ray generator in desirable intensity of radiation. A 1250-curie source will yield approximately 90 R/min. at 50 cm. focal skin distance and at the rate of decay of slightly more than 1 per cent per month, years of practical roentgen intensity will be available. Its disadvantages would be in that the source emits radiation equally in all directions and cannot be turned off; however, with care in design and construction, a satisfactory shielding head and collimating cone may be devised, so that all possible hazards are eliminated. Such a unit, suitable for 1250 C. has been constructed from a basic design of the late Dr. Leonard G. Grimmett. The M. D. Anderson Hospital for Cancer Research, Houston, Texas, and the Medical Division of the Oak Ridge Institute of Nuclear Studies have collaborated in the construction of this unit, which is shown in a schematic drawing in *Fig. 3*. The unit is now completed and is being loaded with a preliminary 200-curie source. It will then undergo exhaustive preliminary studies at Oak Ridge, and will be used in long-term clinical therapy at the M. D. Anderson Hospital when these studies are completed.

SUMMARY

The advantages of radiocobalt over radium have been discussed, and some of the current and potential medical uses have been described. It must be emphasized, however, that a great many of the potential uses are still only possibilities and must await further development. Likewise the availability of radiocobalt is still limited by higher priorities of reactor time and current pile production methods. In summary, the more important advantages of cobalt 60 over radium are listed.

ADVANTAGES

(1) Gamma radiation is simpler, essentially monochromatic, and no filtration is necessary.

(2) There is a reduction in both the primary and secondary electronic emission, so that less shielding is necessary to avoid troublesome local necrosis. This shielding does not appreciably reduce the gamma intensity.

(3) A more homogeneous linear source of radioactivity can be prepared without the danger of "shifting" or localized "hot spots" in interstitial applicators.

(4) It is not necessary to pack the inconvenient powder form of radioactive material

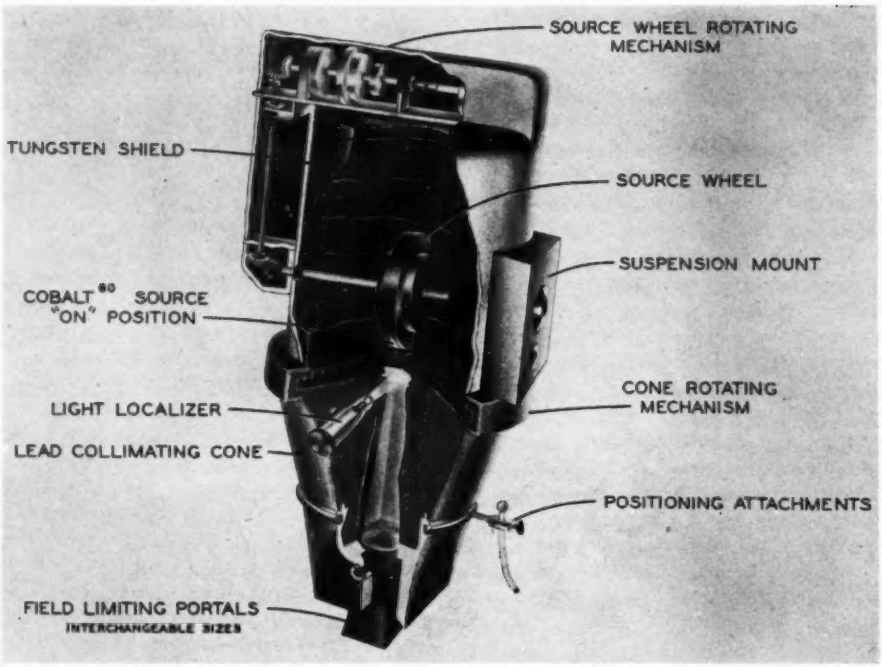


FIG. 3

Schematic drawing of the telecobalt unit constructed by the General Electric Corporation for the Medical Division of the Oak Ridge Institute of Nuclear Studies and the M. D. Anderson Hospital for Cancer Research.

into a container, and the magnetic property of cobalt facilitates handling.

(5) There are no gaseous or inconvenient products of disintegration, and the "radon leakage" problem disappears.

(6) The hazards of radioactivity's being absorbed and retained are minimized, as breakage is eliminated and adequate sheathing can be provided.

(7) Should absorption of radiocobalt in tissue occur, it is rapidly eliminated and not stored in the body, as is radium.

(8) Greater flexibility of treatment is possible with radiocobalt, as a variety of design, shape, and activity may be obtained easily and cheaply for special problems. In a great many instances these may be fabricated before insertion into the reactor, so that excessive handling of radioactive materials is minimized.

(9) High specific activity sources of radiocobalt may be obtained for teletherapy irradiation, which will be far superior to large quantities of radium and compare quite favorably with x-ray therapy equipment in the supervoltage range.

CONCLUSION

Radiocobalt, aside from the obvious financial advantage, has many superiorities over radium in its physical and radioactive characteristics which would make it a more suitable isotope for medical use. Indeed, it is quite possible to agree wholeheartedly with Hahn,[17] who has suggested that "had radium been discovered in the past 5 to 10 years rather than 30 years ago, it would never have been used in the treatment of a single tumor."

BIBLIOGRAPHY

1. Mitchell, J. S.: Applications of Recent Advances in Nuclear Physics to Medicine. Brit. J. Rad., **19**:481, 1946.
2. Coliez, R.: Possible Progress in the Radiotherapy of Cancers. J. Radiol., **27**:177-186, 1946.
3. Myers, W. G.: Applications of Artificially Radioactive Isotopes in Therapy: I Cobalt 60. Amer. J. Roent. & Rad. Therapy, **6**:816-823, 1948.
4. Evans, R. D.: Radioactivity Units and Standards. Nucleonics, **1**:32, 1947.
5. Mayneord, W. V.: Some Applications of Nuclear Physics to Medicine. Brit. J. Rad., Sup. 2, p. 180, 1950.
6. Rutherford, E.; Charwick, J.; and Eclis, C. D.: Radiations from Radioactive Substances. New York: Cambridge Univ. Press, 1930, p. 501—quoted by Mayneord.[5]
7. Quimby, E. H.; Marinelli, L. D.; and Blady, J. J.: Secondary Filters in Radium Therapy. Amer. J. Roent. & Rad. Therapy, **41**:804, 1939.
8. Nickson, J.; Lamerton, L. F.; and Mayneord, W. V.: Absorption of Metallic Cobalt 60 from a Subcutaneous Site. Nature, **164**:613, 1949.
9. Comar, C. L.: Radioisotopes in Nutritional Trace Element Studies II. Nucleonics, **3**:30-42, 1948.

10. Morton, J. L.; Barnes, A. C.; Callendine, G. W., Jr.; Myers, W. G.: Individualized Interstitial Irradiation of Cancer of the Uterine Cervix, Using Cobalt 60 in Needles Inserted Through a Lucite Template. Amer. J. Roent. & Rad. Therapy, **65**:737-747, 1951.
11. Morton, J. L.; Callendine, G. W., Jr.; and Myers, W. G.: Radioactive Cobalt 60 in Plastic Tubing for Interstitial Radiation Therapy. Radiology, **56**:553-559, 1951.
12. Meschan, I.; Edwards, R. R.; and Rosenbaum, P. J.: Practical Physical Aspects in the Use of Radioactive Cobalt 60 as a Radium Substitute. Amer. J. Roent. & Rad. Therapy, **65**:255-264, 1951.
13. Scheer, K.: Quoted by Putnam, J. L.: Radioisotopes Technique Conference, Oxford, 1951. Nucleonics, **4**:5-16, 1951.
14. Low-Beer, B. V. A.: The Clinical Use of Isotopes, p. 343. Springfield, Illinois: Charles C. Thomas, 1950.
15. Grimmett, L. G.: A 1,000-Curie Cobalt Irradiator. Texas Reports on Biol. & Med., **8**:480-490, 1950.
16. Wilson, C. W.: Radium Therapy, Its Physical Aspects. London: Chapman & Hall, Ltd., 1948.
17. Hahn, P. F.: A Manual of Artificial Radioisotope Therapy. New York: Academic Press, Inc., 1951.

DISCUSSION (*Abstract*)

Dr. Gilbert H. Fletcher, Houston, Tex.—I should like to comment separately on the four main uses of cobalt$_{60}$: (1) teleradiators; (2) surface applicators; (3) intracavitary therapy; and (4) interstitial therapy.

Telecobalt irradiators, using a very high intensity source (above 1,000 curies) have been designed to give an output of 80 to 100 r. per minute at 50 F.S.D. These units are qualitatively and quanitatively similar to the 2 Mev. x-ray machines. The purpose of the project is to determine whether telecobalt irradiators will be more economical both in initial investment and maintenance cost, and there is reason to believe that when more reactor space is available, they may become a useful tool in our armamentarium.

The development of surface applicators has always been limited by the lack of availability of large amounts of radium, as well as by the lack of flexibility of the containers. A number of years ago, the South African physicist, van Roojen, devised a theoretical applicator which could give a very homogeneous dose, provided one could spread the radioactive material over large surfaces. With the availability of cobalt$_{60}$, perhaps the "cosine theory" applicators could be revised.

The replacement of radium by cobalt$_{60}$ for intracavitary and interstitial uses is not so simple as many may think. Arguments brought in favor of this substitution are not always put in their proper light. For instance, the leakage of radon, the poor distribution of radium element in the tubes or the needles, the necessity of using 0.5 of platinum to filter the beta rays, and the rigidity of needles are brought as arguments against the use of radium. These arguments are not actually valid. By and large, the inflexibility of the needles is useful in the immense majority of radium implantations, and the thickness of the radium needles has not been proven to cause any significant trauma.

The shortcomings of radium capsules and needles of twenty years ago should not now be used as an argument against the present radium containers. Radon leakage and poor distributor of the radium in the present-day manufacturing of the containers is a very rare occurrence and practically of no significance. The radium salt is now put in thin cells which are placed secondarily in a platinum sheath. When a needle bends or breaks, the small cells usually remain unbroken. The fact that the radium is calibrated in each individual cell produces satisfactory linear intensity.

The fact, which has already been mentioned, that the beta rays of cobalt$_{60}$ are more easily filtered than those of radium has already been demurred with in stating that the necessary thickness of platinum is actually of no significance.

On the other hand, one should not forget that it is quite difficult to obtain pieces of cobalt wire with identical activity. Those who contemplate the purchase of a large stock of pieces of cobalt wire, and who plan to load it themselves either in hyperchrome steel tubing or nylon thread, must have an adequate standardization setup (and physicists) available. The use of cobalt$_{60}$ inside of hyperchrome steel tubing will be in many ways quite similar to the use of radium needles, and the only advantage is the original lower cost of the cobalt needles, as the cobalt$_{60}$ is supplied at a nominal cost by the Atomic Energy Commission.

Differential linear loading of dumbbell cobalt needles can be accomplished somewhat more easily, although this has already been done with ordinary radium element needles. The advantage of the smaller initial cost and therefore, the possibility of a greater variety of needles (some of them with differential loading) might be very easily offset by the fact that there is a decay factor which must be applied. One could not keep these needles very long if one wished to stay within the established range of low intensity gamma ray therapy delivering 6,000 to 8,000 gamma r. within a period of six to eight days. The cobalt$_{60}$ elements could not vary too much from an average intensity and, therefore, could not be used for too long, as they would either be too strong at the beginning of use or too weak at the end. When sets of needles irradiated at different times are acquired, the accounting will become quite complicated and the possibility of error will increase greatly.

The use of cobalt$_{60}$ in nylon thread should be left entirely in the hands of institutions which are fully equipped for constant recalibration and contamination precautions against oxidation products. Nylon thread implantation may have here and there its application, although the great majority of interstitial implantations do not require it, and are even better done with flexible needles.

Some of the other potential uses mentioned by Dr. Kerman are probably valuable, such as the use of spherical sources of cobalt$_{60}$ in tumors of the urinary bladder and special cases of maxillary sinus tumors. Some of the other uses, such as cobalt$_{60}$ in a fluid medium, seem to me extremely dangerous.

In summary, one should keep in mind that cobalt$_{60}$ is not really a new form of irradiation therapy. At its best, it is a cheaper and somewhat more flexible substitute for radium. By and large, it is not going to bring about any radical or even appreciable changes in the treatment of cancer by gamma ray therapy. That it should be investigated and that some of the more elaborate procedures may be valuable is true, but it should be remembered that almost all of the radio curable cancers can be treated adequately with radium, so that more harm than good would come out of rash moves. Radiotherapists, well experienced in the use of radium, should find out the indications of those more elaborate procedures.

Dr. Isadore Meschan, Little Rock, Ark.—We have used cobalt$_{60}$ both experimentally and clinically for the

past three years, and our investigations occurred concurrently with those performed at Ohio State University, independently supported by the Damon Runyon Cancer Memorial Fund and Atomic Energy Commission. We have been reticent to publicize its use in our clinics until we had had the opportunity to investigate basic principles and reactions involved. Our first studies were concerned with the comparative biologic effects of $cobalt_{60}$ as against radium with which we are all familiar. On rabbits' skin, it would appear that in about one-third of the rabbits studied, the cobalt reaction appeared somewhat more quickly and was very slightly more severe than for identical gamma roentgen doses of radium. I shall not dwell on these slight differences since they are of academic interest only, and since these results are in the process of publication now. These slight differences were not anticipated and are of primary interest for that reason. To play safe, we have been subtracting 10 per cent from the gamma roentgen dose that we should use if it were radium we were using, and our clinical responses thus far would justify this rationale.

Apart from $cobalt_{60}$ as a telegamma ray source, I feel that its major usefulness will come in the form of permanent, rigid, low-intensity needles as a substitute for the more expensive similar radium needles. Once fabricated, and standardized, they may be stamped with a dot-dash identification system, and their strength thereafter determined by reference to decay tables. These needles may be used interstitially, in plaques, in intracavitary plastic containers, or in molds as desired. The only significant advantage of these needles over similar radium needles is their low cost to the user. For example, in our own clinic, it has permitted us to acquire the equivalent of 1,000 or 1,500 mg. of radium at a cost of approximately $500.00, whereas a similar amount of radium itself would have cost $30,000 or $40,000. For those clinics that already have adequate quantities of low intensity needles in the form of radium, this advantage would not exist. One must, however, be familiar with the use of radium interstitially in low intensity sources before attempting to utilize $cobalt_{60}$ in this fashion. This general modality of radiation has distinct advantages in certain locations and for certain lesions, but that is another problem which is not up for discussion here.

Morton's nylon tube $cobalt_{60}$ sources have a few advantages and many disadvantages at present. I can visualize that these flexible sources would be of advantage in treating residual carcinoma in the mediastinum at the time of operation, and the like, where a rigid needle could not be left *in situ* and thereafter removed with ease. It has the great disadvantage of being rather cumbersome for the average clinic as Dr. Fletcher has pointed out. These cobalt seeds which are encased in the nylon tubing would require frequent calibration, and constant manipulation, which make their use potentially dangerous from the standpoint of exposure to personnel and contamination from flaking of the wire. Indeed, it would require the employment of a special technician or physicist to load and unload the nylon tubes and calibrate the sources. Such a technician would be expensive, and few such technicians are readily available in this country.

The hazard in the form of flaking of the wire seeds is exemplified by the fact that when I visited Morton last month, his work table was declared too contaminated for further use by the health physicist, and he was to find another location for his ingenious nylon tube loading device. Perhaps a commercial service would help to solve this problem, or gold-plating of the seeds would diminish this hazard, but this is certain to increase the cost of these sources. Hence I feel that the rigid permanent type hyperchrome steel needle which we have devised is superior for routine use, and the flexible nylon tube $cobalt_{60}$ source should be reserved for very special occasions when the more rigid needle cannot be employed.

The type of needle which we are using is now commercially available through Tracerlab, but in their catalogue they have indicated that they are using 19-gauge hyperchrome steel tubing as sheath material, rather than the 16-gauge sheath which we have employed which is approximately the same diameter as conventional radium needles. Needless to say, alteration of the diameter of the gamma ray source will alter the pattern of radiation around the source and depth doses. I am not certain how significant a difference would be introduced by this alteration, but it would have to be borne in mind if these smaller gauge needles are used.

We also have utilized our $cobalt_{60}$ in a modified Ernst-type applicator for treatment of carcinoma of the cervix, and in plastic containers for treatment of carcinoma of the uterine fundus and maxillary antrum. We are in the process of formulating tables for conversion to gamma roentgens for such applicators, since we feel that all dosage should be expressed in terms of roentgens (in a specified time interval) rather than in terms of millicurie hours or milligram hours.

Dr. Charles L. Martin, Dallas, Tex.—I have repeatedly heard the statement made during the past year that radium is no longer useful and that it will soon be completely replaced by $cobalt_{60}$. In my opinion this is definitely untrue. The preparation of $cobalt_{60}$ sources is still a complicated procedure and the danger of contamination of the preparation room is a real one. Then, too, the half life of radioactive cobalt is relatively short and dosage calculations must be changed from time to time. In a busy therapy clinic permanent radium sources render the treatment of patients much simpler and I am not ready to give up my time-tried reliable applicators as yet.

Dr. Edwin C. Ernst, St. Louis, Mo.—We have been very much interested in the depth dose or effective radiation from radium in the treatment of carcinoma of the cervix when employing an expanding type of applicator containing nine 10-mg. quantities of radium in each capsule. We have been able to establish the average gamma-roentgen dose at respectively two and five centimeters lateral to the uterine canal (points A and B) when a total dose of 8,640 milligram hours was administered. I should appreciate knowing how the depth doses compared when a like-amount of $cobalt_{60}$ was substituted. Or, what is the comparative depth dose of a 12-mm. active length radium needle, filtered with either 0.5 mm. or 1.0 mm. of platinum at 5 cm.?

Dr. Kerman (closing).—I realize that any comparison of radium and radiocobalt must necessarily initiate certain controversies and perhaps a reactionary response.

Dr. Fletcher's and Dr. Martin's objections to the relatively short half-life of cobalt, the necessity for more frequent calibrations, and the difficulties of accounting, are well taken. Dr. Meschan has indicated, however, that at least in the rigid permanent needles, these difficulties have been overcome and that radiocobalt is now in routine use in his institution.

Certainly the use of cobalt in nylon tubing as a flexible source has very limited indications, but if the method can be developed so that the hazards are eliminated and the technics of handling and calibration are refined, it, too, may find a valuable place in therapy.

It is quite true that many of the shortcomings of the radium sources that were mentioned are being overcome slowly in the present-day manufacture of these sources. The improvement in precautionary measures in the handling of radium has come primarily as a result of the examples set in the use of artificially produced radioisotopes by the sub-committee on human uses of radioisotopes of the Atomic Energy Commission. However, it is also true that since radium sources are bought, sold, and traded on the open market, there is still sometimes very little attention given to the type or condition of the container. Incidentally, there have been brought to my attention two instances of serious radium leakages which have occurred within the last 6 months, so that perhaps this is not so rare an occurrence as has been implied.

Dr. Meschan has mentioned a possible difference in the biological effect in tissue of radio-cobalt as compared with radium. If this difference is real, certainly more of these studies are necessary so that this information may be applied to dosage calculations.

I think it is to be emphasized that no radical or great change in the treatment of cancer will result from the use of cobalt, but it is possible that this isotope, with further experience and development of its use, may prove to be a more flexible, cheaper, and more desirable form of gamma ray therapy.

The proper evaluation of this usage should certainly be made by radiotherapists who have had considerable irradiation experience.

ANEURYSM OF THE ASCENDING AORTA*

By J. E. MILLER, M.D.
Dallas, Texas

The ascending portion of the aortic arch is the most difficult part of the heart or great vessels to study by conventional radiologic measures. About half of this portion, the so-called root of the aorta, is entirely within the cardiac silhouette. It is not seen in any projection. It cannot be studied, therefore, in the usual manner. As the aorta emerges from the cardiac silhouette, its right border can be seen in the postero-anterior projection. The left border cannot be identified. In the left anterior oblique view the anterior border of the ascending aorta can be easily identified. Its posterior border cannot be seen either fluoroscopically or on films. It is important to realize that the portion of the ascending aorta which is first seen in both of these projections is five or six cm. above the aortic valves. I have seen the diagnosis of syphilitic aortitis or diffuse aneurysm of the ascending arota made on occasions following fluoroscopy and films of the heart. The individuals making these diagnoses say they can see the posterior border of the ascending aorta. I do not believe that two borders of this portion of the aorta can be seen. In my opinion, therefore, these diagnoses are untenable. It is my belief that they are based on the prominence of the ascending aorta which can be detected in both the postero-anterior and left anterior oblique views. This sign alone is frequently seen in older individuals and is due to elongation and tortuosity. If used to diagnose aneurysm or diffuse dilatation of the aorta, it will lead to more errors than to correct diagnoses. In young individuals a prominent ascending aorta is of greater significance in diagnosing aneurysm.

The ascending portion of the aortic arch is the most common site of aortitis. Accordingly, most aneurysms of the various aortic segments occur here. These aneurysms produce few symptoms or signs. In their early stages they cannot be diagnosed or even suspected clinically. They may become quite large and not manifest themselves. If they encroach on the coronary ostia or are associated with aortic insufficiency they may be suspected clinically. This paper is a discussion of a large number of aneurysms of the ascending portion of the aortic arch. Most were not suspected clinically. Many were not suspected by conventional radiologic procedures. An unequivocal diagnosis can seldom be made by ordinary radiologic procedures. Those with sufficient calcium in their walls can be diagnosed by plain films. Angiocardiographic examination is required to diagnose aneurysm in most of these patients. The angiocardiogram was done because an abnormality was known to be present but its nature not always suspected.

*Read in Section on Radiology, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

*From the Department of Radiology, Baylor Hospital and Southwestern Medical School of the University of Texas, Dallas, Texas.

The usual aneurysm of the aorta is saccular. By definition an aneurysm should be a sac. It is my opinion that all of the dilatations of the aorta should be called aneurysm. Various types of "aneurysmal dilatation" of the ascending portion of the aortic arch will be shown.

Jackman and Lubert[1] showed that calcification of the ascending portion of the aortic arch occurs in patients with syphilitic aortitis. In fact, when seen it is good evidence that syphilitic aortitis is present. The calcific aortic sclerosis seen almost routinely in patients over 60 occurs only in the transverse and descending portions. Many of these patients with calcification of the ascending portion have diffuse dilatation and others large saccular aneurysms. When sufficient calcification is present the aneurysm can be easily diagnosed by conventional films. Stratagraphs have been useful where the usual films do not show the calcification well. *Fig. 1* shows a curvilinear calcific plaque in the lateral wall of the ascending aorta. The slightly left anterior oblique film which is overexposed shows calcium in both walls and shows the aneurysmal dilatation of this portion of the aorta. Many similar cases are available for study. In several cases the fusiform aneurysm of the ascending aorta is several cm. in its greatest diameter. In the lateral or left anterior oblique projections the linear calcification marking the posterior wall is clearly visible. When the entire wall contains sufficient calcium an accurate estimation of the size of the aneurysm can be obtained.

Several calcified tumors in the anterior mediastinum have been seen. In one of these individuals the calcified mass was seen only in the lateral projection. Several postero-anterior projections were obtained with varying technic but on none of these was the mass detectable. Because of the controversy as to whether this represented an aneurysm or a dermoid cyst angiocardiograms were performed. The aneurysm was quite adequately demonstrated on the angiocardiogram and it was noted that it displaced the main pulmonary artery to a significant degree. This phenomenon has been observed several times in various types of ascending aortic aneurysms. In fact, in one of these, the pressure

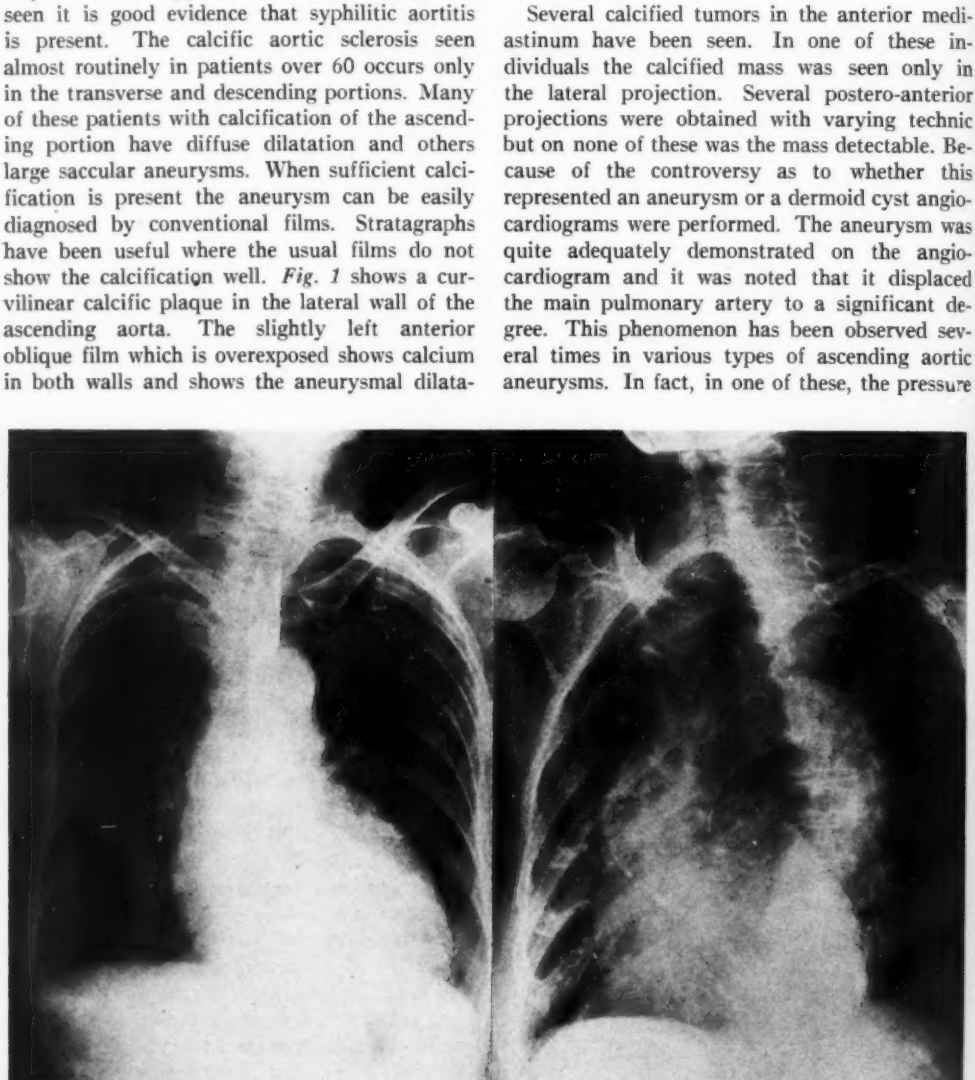


FIG. 1

Calcification of the ascending arota with diffuse aneurysmal dilatation.

on the pulmonary artery was so great as to be considered the cause of pulmonary artery obstruction with right ventricular hypertrophy (cor pulmonale).

Not all of the aneurysmal dilatations of the ascending aorta are due to syphilis. One we have seen frequently is that which occurs with coarctation of the aorta. Conventional films frequently show a prominent ascending aorta. Many of the angiocardiograms we have on this condition show a diffuse dilatation of the ascending aorta. *Fig. 2* shows the notching of the ribs indicative of coarctation. Even in this young man the ascending aorta is quite prominent. In addition to the dilation the angiocardiogram (*Fig. 3*) shows the coarctate segment and the internal mammary arteries. The disproportionate left ventricular enlargement is well shown in this view.

Two children have been seen with aneurysm of the aorta. The aneurysm has been chiefly the ascending portion of the aortic arch. Both have had Marfan's syndrome. These patients usually have arachnodactyly, dislocation of the crystalline lens and congenital heart disease.

FIG. 3

Fusiform aneurysm of ascending aorta seen frequently in coarctation.

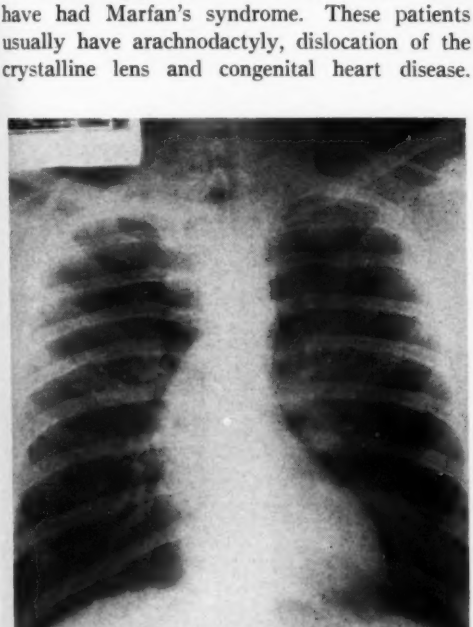


FIG. 2

Prominent ascending aorta in young patient with coarctation.

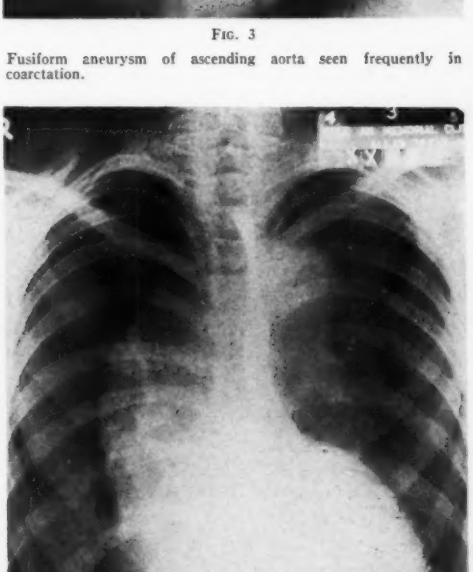


FIG. 4

Aneurysm of ascending aorta in a child with Marfan's syndrome.

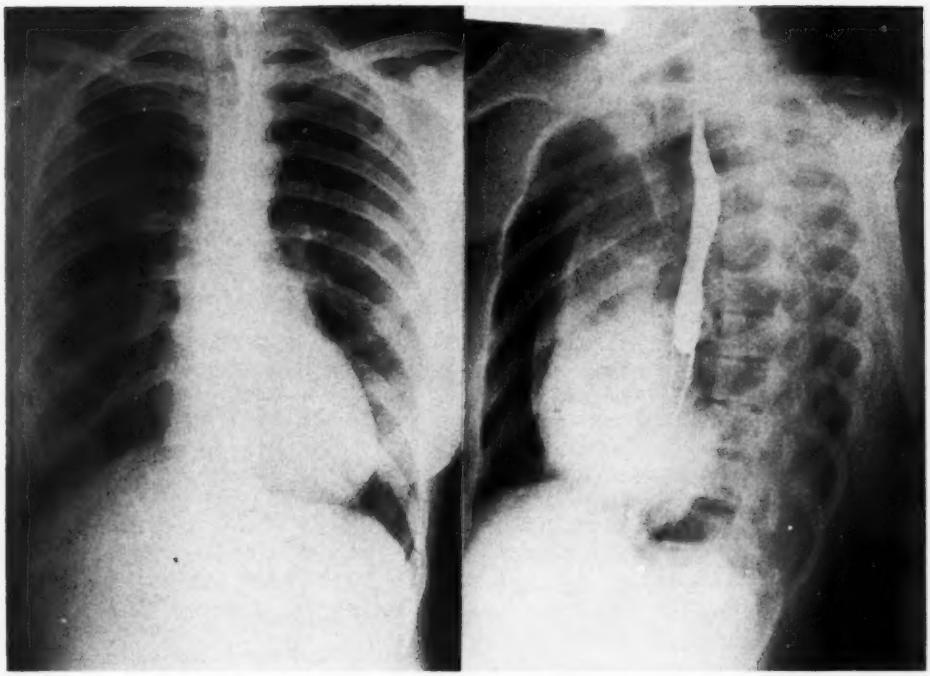


FIG. 5

Slight prominence of ascending aorta in postero-anterior film of young woman with aortic insufficiency.

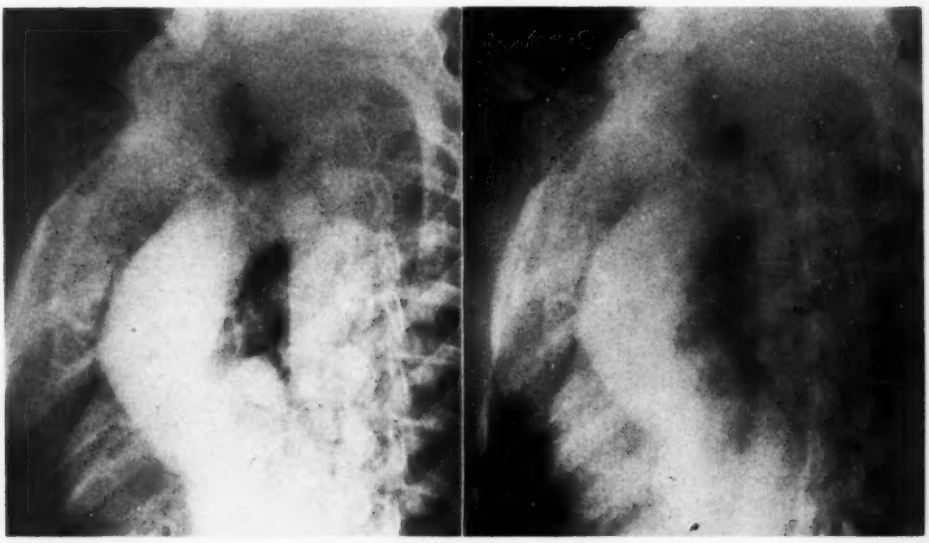


FIG. 6

Fusiform aneurysm of ascending aorta. Same patient as *Fig. 8*.

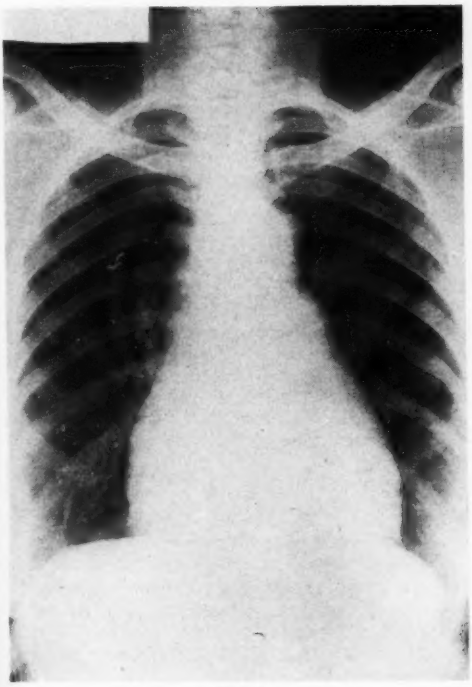


FIG. 7
Moderate cardiac enlargement. Aortic aneurysm not suspected.

Medial necrosis of the aorta occurs with resulting aneurysm. *Fig. 4* shows such a case with rather extreme dilation of the ascending aorta.

Fig. 5 shows the ascending portion of the aortic arch to be prominent in a 22-year-old woman. At this age, this appearance is significant. This is especially true in the presence of aortic insufficiency. Disproportionate left ventricular enlargement is quite apparent in the left anterior oblique view. *Fig. 6* shows the sixth and seventh films of the angiocardiogram with the obvious diffuse aneurysm. This aneurysm was suspected from conventional roentgen studies. The contrast material affords adequate proof of its presence.

A similar diffuse aneurysm of the ascending portion of the aortic arch has been seen which is of particular interest. This patient, a Negro man, was also in the third decade of life. Conventional films showed nothing suggestive of abnormality of the heart or aorta. This patient had a most unusual clinical finding. No murmur could be heard by ordinary auscultatory procedures. With the patient on the left side a loud diastolic murmur was heard in the aortic area. It was so sharply localized that it was not heard when the bell was moved the distance of

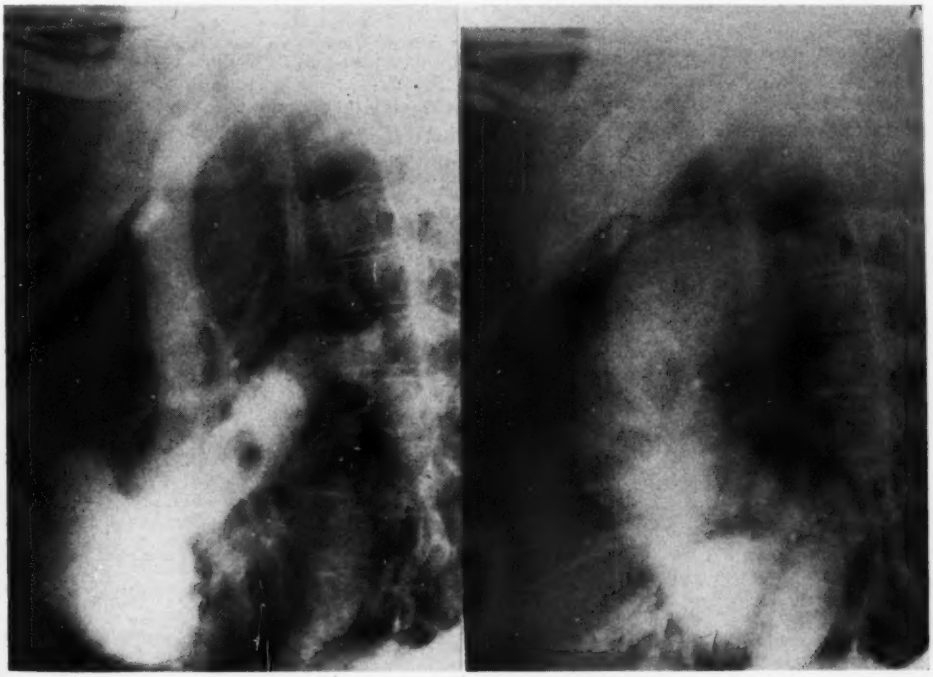


FIG. 8
Large aneurysm of aorta with posterior displacement of pulmonary artery. Same patient as *Fig. 11*.

its diameter. It is my opinion that in this position distortion of the aortic root and its valves permitted aortic insufficiency. After experience with this patient it is obvious that all valve areas should be examined in this position. The angiocardiogram was practically identical with that seen in *Fig. 6*.

Fig. 7 shows the cardiac silhouette to be obviously enlarged. No definite diagnosis could be made with all the clinical and roentgen data. Aortic aneurysm was not suspected. *Fig. 8*, the angiocardiogram, shows the pulmonary artery to be displaced posteriorly by an anterior mass. This mass is well demonstrated to be a large aneurysm of the ascending aorta. These two films demonstrate the close association between the pulmonary artery and the ascending aorta.

One other type of aneurysm has been of particular interest to us. This particular patient had an obviously enlarged heart which was well demonstrated in two projections. An angiocardiogram previously failed to make an accurate diagnosis. Clinical efforts also failed. The first two films of the angiocardiogram showed the pulmonary artery to be displaced forward and upward. The subsequent films showed this mass to be a large saccular aneurysm of a sinus of Valsalva. This is one of the most unusual aneurysms we have seen. In reviewing a rather voluminous chart a note by Dr. Tinsley Harrison suggested this possibility some four years ago. This is one of several suggestions, however, and his reasons for making it are not clear.

CONCLUSIONS

(1) Many aneurysms of the ascending aorta cannot be diagnosed by ordinary measures.

(2) Many previously unsuspected aneurysms of this portion of the aorta have been discovered by angiocardiography.

(3) The root of the aorta can be seen on conventional films only when calcification is present in the opposing walls.

REFERENCE

1. Jackman, James: and Lubert, Mortimer: The Significance of Calcification in the Ascending Aorta as Observed Roentgenologically. Amer. J. Roent. and Rad. Ther., **53**:432-438 (May) 1945.

DISCUSSION (*Abstract*)

Dr. E. W. Spackman, Fort Worth, Tex.—Most of us have had the experience of exhausting conventional means of diagnosis without being able to identify a mediastinal mass as tumor or aneurysm and have, at a later date, regretted that we did not possess some more positive method of approach, when the surgeon has opened the chest and discovered an aneurysm. This type of procedure is the answer to the problem in those cases wherein doubt remains after thorough work-up.

Doubt exists in a fair proportion of cases in spite of complete work-up from clinical and radiological standpoints. Although kymography and tomography will, at times, give contributory evidence, they also fail to establish differential diagnosis in the type of case under discussion. We believe that one of the special procedures with opaque dye is definitely indicated in selected cases before operative exploration.

We have used angiocardiography by the method described, but have preferred aortography, approaching through the carotid and inserting a catheter under fluoroscopic control into the ascending aorta. Injection is made similar to that for angiocardiography with a run of 5 or 6 frames on the Fairchild apparatus. We believe this gives somewhat stronger contrast and better visualization.

The described methods are certainly a forward step in differential diagnosis of these very baffling problems.

SOME CONSIDERATIONS REGARDING LONG-TERM REHABILITATION OF BRAIN INJURIES*

By BEN L. BOYNTON, M.D.†
and
L. A. LEAVITT, M.D.‡
Houston, Texas

In considering the problem of long-term rehabilitation of brain injuries the first goal of the physician is to save the life of the patient. This is obvious, and it is not our purpose in this discussion to consider the supportive measures that are required in the management of the acute or subacute phase of the brain injury case. Rehabilitation of the patient with severe brain injury begins at an indeterminate time following the injury, but generally may be said to commence when the patient has become sufficiently lucid to understand some of what is being attempted. For example, it will be noted in the cases we are about to present that the patients

*Read in Section on Physical Medicine and Rehabilitation, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

*Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

†Chief, Physical Medicine and Rehabilitation Service, Veterans Administration Hospital, Houston, Texas.

‡Assistant Chief, Physical Medicine and Rehabilitation Service, Veterans Administration Hospital, Houston, Texas.

were aphasic, were displaying decerebrate meaningless movements of the extremities and some had difficulty in swallowing. However, at this stage of recovery the implementation of treatment with attempted beginnings at speech re-education, attempted active assistive exercises with purposeful movements and such other bedside measures as might seem indicated appear to have a very definite place in the restorative approach to these patients.

The following brief case histories are presented to give a word picture of the patients about whom we are centering our discussion.

Case 1.—L. P., age 25, was a derrick man in an oil field. He had been in the Army, 1943 to 1945. Later he was engineer in a butane plant. He was injured in an automobile accident June 17, 1950, with a fractured left femur and head injury. He was initially hospitalized for three weeks at Baptist Hospital, Beaumont, Texas. The prognosis was grave, and he was transferred to the Veterans Administration Hospital, Houston, Texas, on July 12, 1950, was admitted to orthopedics, then transferred to neurosurgery.

He was comatose from the onset of injury until August 8, 1950, a time of seven weeks, and the prognosis was so grave that reduction of the fractured left femur was not attempted. He had a fracture of the right frontal bone of the skull; contusion and laceration of the right parietal area with incomplete lesion of the midbrain; and bilateral talipes cavus. He was transferred to physical medicine rehabilitation service on September 1, 1950. However, on August 8, 1950, he spoke a few words for the first time. He was placed in a wheelchair for progressive lengths of time, and on August 25, 1950, bedside physical therapy and educational therapy were started which included early retraining in communication by educational therapy and active assistive neuromuscular re-education to the involved extremities by a physical therapist. At this time the patient was bed and wheelchair status, confused, disoriented and partially aphasic with gross incoordination, paralysis and weakness of the musculature of the extremities. He was enrolled in educational therapy for retraining of speech (communicative education) and corrective therapy for progressive resistive and coordinative exercises of involved musculature in preparation for ambulation utilizing crutches. By October 10, 1950, he was able to walk a distance of 15-20 feet in the walker and also able to answer questions about himself, environment, and family without error and less hesitation, comprehension improving, and he was able to read newspapers. His speech still was of scanning nature, nasal in quality. At this time he was ready for placement in therapeutic situations of purposeful activities and in environments where resocialization with other patients would occur. Therefore, group work in educational therapy was started and also occupational and manual arts therapy.

From time to time he showed a tendency to become strangled on food and liquids, due to incoordination of the swallowing mechanism. Incoordination was also present in the lower extremities.

By April of 1951, ten months after injury, the patient was able to walk on crutches for longer distances, able to sit in a chair, rise from a chair unassisted and perform other activities of self care, and, therefore, was transferred to the ambulatory ward. (In this type of ward the patients ambulate to the mess hall, make their own beds, *et cetera*, and if one patient is more handicapped than another, he receives help from his fellow patients in performing activities of daily living, thus duplicating as far as possible within a hospital the environment of the patient's home and the problems of resocialization). The patient was placed on extended leave status to his mother's home on June 8, 1951, and on monthly reexaminations it was noted that he made satisfactory progress in ambulation and return of speech and memory.

On August 6, 1951, he was re-hospitalized and was fitted with orthopedic shoes to give support to his ankles because of residual weakness and incoordination and to make him ambulatory with a cane. He was discharged to be followed on non-bed occupancy status for the next twelve months. At this time he was able physically and mentally to do manual labor of simple repetitious movements in a sitting position or small chores about the home such as garden work, dishwashing and running errands.

Case 2.—K. A., age 57, an electrician and mechanic, was injured in an automobile accident January 4, 1951. He was admitted to a local private hospital immediately following the accident and transferred to the Veterans Administration Hospital, Houston, Texas, on January 26, 1951, to the care of the neurosurgery service. On admission, he showed: contusions around the head but no evidence of skull fracture, was semicomatose, had occasional nystagmoid movements to the left and there was drooping of the left corner of the mouth. He was unable to speak and possibly unable to understand spoken words. There was weakness and reflexes were absent in the right arm. Abdominal reflexes were absent and probably ankle jerks were negative. The impression was of trauma to the left cerebral hemisphere, including the temporal lobe and motor cortex. Observation and supportive treatment were advised.

The patient was semicomatose at the time of admission to the hospital. He was placed on tube feedings of a high protein diet, crystacillin® 300,000 units daily, and was turned from side to side every two hours with aspiration of pharyngeal mucus. A spinal tap on admission revealed initial pressure of 140 mm. with crystal clear spinal fluid containing 6 red blood cells, 12 polymorphonuclears and 3 lymphocytes per cu. mm. It was learned from the hospital in Weimar that the patient had initially shown bleeding from both ears and the nose, right hemiplegia and grossly bloody spinal fluid, which gradually cleared.

The patient ran an intermittent fever to 102° during the first three weeks in the hospital but this returned to normal and he gradually began to show more response to his surroundings. He was up in a wheelchair three times daily and attempted to eat but showed some difficulty in swallowing so that tube feeding had to be continued. He began going in a wheelchair to corrective therapy on March 8, 1951. He was able to stand up in a stationary walker for only a few seconds before his legs gave way. He continued to stand in corrective

therapy for increasing amounts of time and was gradually able to walk in the stationary walker. Educational therapy was begun on March 8, 1951. He was able to name various test objects. Initially he mumbled and showed difficulty in concentrating for more than a few seconds. He was transferred to the physical medicine rehabilitation service April 17, 1951 (4½ months after injury) for intensive rehabilitation. At this time he was able to take food by mouth but sometimes he was unwilling to do so. He would go without eating for several days and, therefore, tube feeding was resumed. He had to be restrained at this time to prevent his pulling the tube out. It was learned that his wife had been operated upon at about the time the patient was transferred to the rehabilitation service. He, of course, had not been told the reason why his wife was not visiting. As soon as the wife's condition was found to be satisfactory, the patient was told of her operation and was told that she would visit as soon as she was well enough. Although he displayed very little emotional response, he seemed more cooperative thereafter. For no apparent reason he began to take food by mouth regularly and in large amounts on April 26, 1951. Thereafter he displayed a tremendous appetite and began to gain weight. He gradually learned to ask for the urinal or to go to the bathroom whenever necessary. A patient in the next bed was extremely helpful in reminding him about these matters. He made steady improvement in educational therapy, corrective therapy and on the ward. He was started in manual arts therapy for electrical work on May 16, 1951, but seemed unable to follow even simple directions. By June 6, 1951, the patient was fairly well oriented, cooperative, displayed complete control of bladder and bowels, was ambulatory on the ward, and was capable of complete self-care including shaving himself. He still displayed occasional confusion as to where he was and frequently greeted other patients with Bohemian names belonging to friends of his in Weimar, Texas. His wife had visited frequently by this time and other relatives had also been instructed as to what might be expected in his behavior. He was given a therapeutic leave of absence on June 6, 1951. As expected, he showed fewer periods of confusion in his own home than in the hospital. As he had shown some interest in electrical work in manual arts therapy, he was encouraged to continue this at home. At first he was unable to concentrate for long enough to accomplish a given task without assistance. His ability to concentrate gradually improved so that his wife reported that he had repaired a number of things around the house while on leave. The wife also reported that he enjoyed reading the newspaper and seemed to understand what he read. He was followed at 29-day intervals on a leave status until August 31, 1951. At this time he was re-examined and showed very little weakness of the right leg, slight weakness of the right arm and some residual pain and limitation of motion of the right shoulder. This was felt to be secondary to the right hemiparesis which was present initially, but x-rays were taken to rule out the presence of fracture. These were reported as negative. A repeat complete blood count, serum test, urinalysis, and chest film were negative or within normal limits. He appeared mentally alert, cooperative and cheerful, and walked without a cane. He was discharged as having maximum hospital benefit on August 31, 1951.

Case 3.—R. M. A., age 35, a ranching and manual laborer (40 per cent disabled by duodenal ulcer) had an automobile accident May 26, 1951. He was hospitalized immediately at a local hospital and transferred to neurosurgical service, Veterans Administration Hospital, Houston, Texas, May 31, 1951.

On admission he showed right hemiparesis with no evidence of skull fracture, was semicomatose and restraints were necessary on the left arm to permit tube feeding. He had motor and questionable sensory aphasia. There were superficial abrasions. The impression was of cerebral laceration of the left hemisphere in the region of the postsylvian fissure.

In the hospital, the patient was given lumbar puncture and supportive treatment. The spinal fluid was essentially normal. Tube feeding and restraints were continued for approximately two weeks.

On June 15, 1951, (three weeks after injury) the patient was transferred to rehabilitation service for an intensive restorative regimen consisting of physical therapy for active assistive and passive movements of the right upper and lower extremities and educational therapy for speech retraining (communicative education). He was also assigned to occupational therapy for improvement of gross movements of the right upper extremity. Psychometric studies showed an intelligence quotient of 76. He did not respond well to situations which were difficult for him to interpret (Rorschach) nor did his responses indicate ability to learn with any ease. He worked best in a restricted situation in which tasks placed before him were highly structured and the solution was easily found.

Speech retraining was discontinued after three weeks of treatment as he was able to communicate quite adequately. Return of function in the right lower extremity was relatively rapid and he was able to ambulate with the aid of a cane by July 23, 1951, and gave up the wheelchair within two more weeks.

Progress in occupational therapy in regaining gross to fine movements of the right upper extremity was satisfactory until August 27, 1951, when the patient became emotionally upset due to the failure of his family and friends to visit him. He interpreted this as rejection by everyone, including doctors and therapists. However, with reassurance he gradually resumed therapeutic activities. (His mother had failed to visit because she had been hit by a cow!). Further convalescence was uneventful and he was discharged completely capable of self-care on October 5, 1951.

The three cases presented above are representative of about ten similar patients we have treated or are now treating. The difference in severity of the head injury reflects directly the duration of the recovery period. It is possible to predict with fair accuracy that convalescence will be prolonged in a geometric relationship to the severity of the cerebral trauma. However, the important prognostic feature is the generally favorable outcome should the patient survive the period of coma.

Another factor which has become increasingly apparent to us is the importance of fellow patients' taking an interest in the convalescing head injury patient. The importance of the friendly interpersonal relationship thus established is a very cogent element in augmenting social consciousness. Simple things are achieved such as encouraging the patient to bathe, shave and attire himself properly, also stimulation of proper and regular eating and excretory habits. All of these add up to a more socially accepted and better adjusted patient. Another by-product of real worth is the pleasure attained by the interested fellow patients who rightly feel that they are making a significant contribution to human welfare.

In conclusion we have presented three illustrative cases of severe head injury whose progress toward a return to productive living has been stimulated by:

(1) Excellent supportive therapy during the acute and subacute phase.

(2) Early installation of bedside activities designed to augment the patient's returning awareness of himself and others.

(3) Opportunities for increased activity of the patient under therapeutic guidance designed to facilitate resumption of responsibilities by the patient himself.

(4) Other patients' interest in and assistance of the head injury patient.

SURGICAL TRAINING FOR THE GENERAL PRACTITIONER*

By RANDOLPH T. SMITH, M.D.
Little Rock, Arkansas

We, the physicians of this country, are today faced with a serious moral and economic crisis. We have been accused of failure to furnish adequate medical care to all the people, and under the guise of trying to compensate for this so-called failure, the planners of our national economy have launched a campaign to take over, control, and direct the medical economy of this nation. The doctors of the United States, both through the untiring efforts of a multitude of individuals and through the vigorous campaign conducted by the American Medical Association, have just recently, and, I fear for the time being only, forestalled the effort on the part of the present administration to nationalize our profession. Such a nationalization of medical care has already taken place in Great Britain and has resulted in a sort of professional peonage that has brought about a lowered income and standard of living for the doctor, and a downgrading of patient care that has become a national shame.

Except for the accusation that our fees are unmercifully high sometimes, there has been not too much criticism of either the quality or availability of medical care in the cities. We have been particularly charged with failure to provide adequate medical care for the rural and sparsely populated areas of our country. The advocates of nationalization of medical care say that rural health has suffered because of our failure to take care of these less populous and prosperous communities.

Far and near one hears the cry that there are not enough doctors in the land. The farm groups are particularly vociferous in this respect, and their protestations have lead the vote-seeking politician to demand the establishment of more and bigger medical schools, in order to turn out more and better doctors. Most of the 72 recognized medical schools in the country are already in financial trouble. This has caused the planners to declare that private enterprise has failed again and it is time for the government to step in with federal subsidy and keep the medical schools going and turn out more doctors. Medical education is admittedly expensive; but what the government helps, it also wants to run.

The difficulty is not a matter of shortage of doctors, but a matter of distribution and training. The better trained men naturally gravitate to the larger centers of population where hospital facilities are available and their work is easier and more lucrative. Only under a system of dictatorship can a man be made to go where he does not want to practice.

Several months ago in the city in which I live we had a very fine meeting. It was a statewide rural health conference, promulgated by the president of our state medical society and attended by some six hundred laymen, and, perhaps, seventy-five doctors from over the state. There were talks by leaders in the medical society and by prominent laymen. The president of the State Farm Bureau Federation spoke. The

*Read in Section on General Practice, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

next day the morning newspaper, in large headlines, ran this lead: "The People Talk Back To The Doctors!" It quoted the Farm Bureau man as saying that the doctors of the state should be chastised because of the way they charged their patients. He also made the statement that the doctors of the state could discourage the advent of "socialized medicine" if they would change their ways and furnish to the rural citizens of the state adequate medical care and adopt and follow a reasonable schedule of fees.

Our governor, speaking this past month at the opening ceremonies of our State University School of Medicine, said that it was up to the doctors themselves to prevent socialized medicine from coming into the state and elsewhere, and suggested that the solution would be to give more particular attention to the rural areas where medical facilities are lacking. He urged the graduates to stay at home and help more in the rural communities.

Now, the question is, what constitutes adequate medical care? The way we doctors answer that question will determine how we discharge our moral obligation to the people of America. Just as the president of the Farm Bureau Federation and the governor of our state suggested, failure to answer this question promptly and properly is to invite the government to step in and try to solve the problem by nationalizing the practice of medicine. I see no reason why we cannot solve this problem among ourselves, and my particular interest is in the specialized training of the men who are to go to these rural communities. I am speaking of the training of the general practitioner and the part he must inevitably play in bringing this adequate medical care to the people of these United States. I am especially interested in his surgical training.

There is not a large city in this country that does not constitute a center of medical availability. There is not a city of 100,000 population, or more, that is not equipped to take care of practically any medical, surgical, or obstetrical situation or emergency, both because of its well-equipped hospitals, and because of the fact that these hospitals are well staffed with specialists in practically every line. There may not be enough hospital beds in these cities, but, certainly, there are enough well-trained doctors.

But the majority of our people live in rural communities and in small towns, where hospitals have been small and widely separated, and where one seldom finds a specialist in any line. Hospitals are expensive to build and more expensive to maintain and operate. It will cost a doctor thirty or forty thousand dollars to complete his basic education in a good school and then he must spend four or five years getting a specialty training. He has become accustomed to working in a well-equipped hospital, frequently getting what Sinclair Lewis called the "hospital virus," and is unwilling to go to a small community, particularly if it has no hospital. A rural practice does not attract him either socially or financially, and he has very little patience with the country doctor.

The doctor in the city, who is a specialist, has very little understanding of the problems of the small town doctor. He feels that the latter is not capable of being anything other than a family doctor, whose function is to make house calls, do an office practice, and drum up business for him, the specialist. The rural doctor may give pills and try for a diagnosis, but if treatment is to be given, the patient should be sent into the city to him, the specialist.

Many surgeons certainly feel that the rural and small town doctor should do no surgery. But surgery, and often very good surgery, for years has been done and will continue to be done by them, whether we like it or not. In times past, in the back stretches of the land, many a life has been saved through kitchen table surgery. In fact, I used to hear Dr. Howard A. Kelly, whose surgical training and ability cannot be questioned, tell of the many times he has done kitchen table surgery in many a south Baltimore home.

The doctor in a small town or rural community is a general practitioner, and I mean just that. He takes his patients as they come and treats them for whatever ails them. Most of his practice is office and home work, mostly medicine. In a strictly rural community he covers much ground, delivers many babies, and dispenses his own medicine. The small town doctor may do his deliveries in the home, and minor surgery in his office. Until a few years ago, hospital facilities were not available to him. A few doctors had two or three beds at their offices, where they put tonsillectomy cases and, sometimes, their obstetrical cases after delivery. Sooner or later, every doctor who had a few

beds in his office called his establishment a clinic. If he had difficult surgical cases, he would send them to the city to a specialist. Whenever nearby towns had small hospitals, he might take his patients there and do the surgery himself, or get one of his more experienced colleagues to do it for him. His patients did not demand much in those days, and the large farm organizations, the powerful unions, and the government planners had not come into being.

But times have changed. Life is faster and people have become more demanding. Small hospitals have sprung up all over the country during the past two or three years. In our state, under the benefits of the Hill-Burton Act, 12 hospitals have been completed in the smaller towns and 12 more are in the process of being built. In the 12 completed, there are now available 515 beds; the 12 under construction, when completed, will add 487 more beds, making a total of 1,002 beds. The smallest will have 29 beds, and the largest 100 beds. This bed capacity is almost twice that of the total bed capacity of the private hospitals in the capitol city of our state. These hospitals are located in towns varying in population from 2,000 to 20,000.

One of my colleagues, a very fine surgeon, looks upon these new hospitals with considerable misgivings. He feels that these hospitals give the citizens in the community a false sense of security. They look with pride upon the bright shining equipment in the operating rooms, the row upon row of new white beds, and the awe-inspiring laboratory and x-ray equipment and feel that their health and happiness are now secure. They have the fine hospital, but have they the trained men to staff it? My surgeon friend feels that they may not. As he puts it, he feels that the physical availability of these new hospitals will "embolden many improperly and inadequately trained doctors to do surgery," surgery which they are not capable of doing.

There is an element of truth in his statement. The daughter of a friend of mine married a young doctor who did not finish his internship. He quit in the eighth or ninth month of his service to accept the very attractive offer of a practice in an upstate rural community. He did a general house and office practice for a couple of years. He sent his surgery to the nearest good surgeon in a center about a 100 miles distant. Well, we had a football game here the other night. The young doctor could not come down with his wife to see the game, as he had done an appendectomy that morning, his first one, and could not leave. A new Hill-Burton hospital had just been opened in a small town some 10 or 12 miles away and he had availed himself of this opportunity to launch himself as a surgeon. A general practitioner friend of mine in a town of 18,000 wrote me the other day that the first thyroidectomy he had ever seen, he did himself. This takes courage, but courage and capability are not one and the same.

Just who should do surgery? I have asked many of the surgeons in my community this question. They all agree on one point: no one should do surgery who is not capable of doing surgery. What makes a man capable of doing surgery, I then ask? Adequate surgical training, is the surgeon's answer. There are those of my friends who feel that no one should do surgery but the surgeon who has had at least five or six years of resident training. All say that no man should open an abdomen, for example, unless he is capable of performing any procedure within the abdomen. All feel that a man's conscience should tell him whether or not he should attempt a surgical procedure. One of my friends, who did a general practice for years, mainly because he was in a community where there was no hospital, says no general practitioner should attempt to do any surgery more extensive than lancing an occasional boil, or putting a few clips in a superficial skin wound. He now lives in our city and devotes himself to doing the surgery for a clinical group.

Recognizing the inescapable fact that the general practitioner is going to do surgery anyway, one of my friends, who had a seven-year surgical residency, says he sees no reason why the general practitioner in the small town should send him appendectomies, hernias, gallbladders, and the like. He says he expects only the more complicated cases such as pneumonectomies, the more difficult cases of bowel surgery, arterial surgery, and the like.

A different attitude prevails in the small communities as to who should do surgery. The people have confidence in their doctors. They do not expect them to be specialists, but they do expect them to take care of the ordinary surgical emer-

gencies as they arise. I feel that the man who does a rural and small town practice should have the training adequate for the demands of his community. I believe everyone will agree that no doctor should attempt anything he feels he is not capable of doing, but it does not seem to me that a man should be a Mayo or a Halsted or an Ochsner in order to do the routine surgery which he finds in his general practice in the smaller communities having adequate hospital facilities. And it is the moral obligation of our profession to see that this man is well trained, and it is the responsibility of medical educators to implement such a program.

What should this surgical training be? Before answering this, let us view for a moment the background of surgical training as we know it today. Lehman, in a recent article[1] in the *Journal of the American Medical Association*, gives these major steps in its development: first, the principles of adequate surgical training and the principles of the resident system as promulgated by Halsted 60 years ago and which stand almost unchanged to this day; second, the principle of the closed-staff hospital, which early in this century revolutionized the practice and quality of hospital surgery; and, finally, the regulation of hospital staff activity through the agency of the different accrediting boards. I went to school in the East where the closed-staff and resident systems were in force. My school enjoyed along with its teaching hospital a fine reputation that is still world-wide. The names of my professors and the heads of the various departments in the hospital were known throughout the civilized world, but each service turned out only one resident a year. Some years the surgical service did not turn out a resident at all, if the incumbent decided to stay on another year. In the twenty-five years since my graduation, only a couple of dozen or more surgical ex-residents have been sent out from that teaching hospital, and not a single one of them has settled in a small community. Most of them, in fact, have, and with considerable justification, become full-time teachers in other medical schools and hospitals. These men are all surgical specialists and now act as judges, so to speak, in a court of last appeal in the populous communities in which they are located.

Should our hospitals be open only to men who have had such highly specialized training? There will not be enough of them to be distributed among the thousand or more Hill-Burton hospitals soon to be found throughout Smalltown, U. S. A., and the five or six hundred more such hospitals being built in the larger centers. These superbly trained men have gone and will continue to go to these large city hospitals, which, perhaps, is where they should go. The general practitioner in the smaller community, recognizing his limitations, knows that he can refer his more difficult cases to these more highly trained men with safety to his patients and honor to himself.

Sufficient time has not elapsed to reveal just what regulatory demands will be made by the Federal Security Agency in the operation of the hospitals built under the Hill-Burton plan. Some regulation is certain. If it is coupled with the principle of closing the staffs of hospitals to all but diplomates of the various specialty and accrediting boards it may result in a very high type of surgical, medical, and obstetrical practice, but will create an intolerable situation from the standpoint of the man who is not a product of the present resident system and one that would be quite impractical in the small hospitals. Nor would it operate to the best interest of the public.

Of what should the surgical training of the general practitioner consist? In my opinion, the basis of all training should be a first year of rotating internship. This gives the graduate a chance to orientate himself. From then on there are several plans. One plan proposes a second year of instruction in the basic sciences, chemistry, physiology, anatomy and pathology, with x-ray as a clinical tie-in. The next year would be devoted to the outpatient department part of the day, and the operating room the rest of the day. A fourth year would be devoted to a sort of country practice consisting of work in the wards and in the operating room, work in the delivery room, and an assignment to cases by rotation of admissions to the three major services, medicine, obstetrics, and surgery.

Another plan provides for the first year of rotating service, then for the following three years, a rotation every six months between the basic sciences, including laboratory work, and the operating rooms, delivery rooms, and the

wards. A third plan starts out with the year of rotating internship, one year of specialty training in surgery, outpatient clinics, operating rooms, obstetrical department, and, then, a farming-out to small, recognized hospitals in the small towns and rural areas under the direction of designated general practitioners of recognized ability. During this farm-out period, they serve both in the community hospital and in the offices of the general practitioners under whose guidance and direction they are working. None of these plans is perfect, but they are all being tried out.

A number of university hospitals have advertised these plans. There have been few takers. The idea has not particularly appealed to the medical school graduate. In one university hospital, where the plan of farming out the second- or third-year resident was tried, the result was almost disastrous. The men who were farmed out discovered that they were doing the same work in these small hospitals as the private practitioner, but were not getting the pay. The temptation was too great; they quit almost to a man, and, severing their connection with the university, took up private practice as general practitioners in the community, and did not return to the parent hospital. The next year, that particular university hospital had no applicants for its course in general practitioner training.

Perhaps four years is too long. I certainly feel that the period of diversified specialty training should not be less than two years. There are a number of two-year services. Some states permit a man to do any type of practice immediately upon graduation from medical school. These men usually do a general home and office practice for a couple of years, then gradually branch out. These men can be taught to do surgery through a sort of on-the-job training program. A few days ago I was discussing this subject with one of my colleagues, who has one of the largest surgical practices in town, and who also does a very active office practice. It was his feeling that the young doctor doing a general practice and wanting to do surgery, but feeling himself inadequately trained, could secure such training by what Bibler of Indianapolis calls "self-education."[2] His proposal was that any young, general practitioner here in our city could come to his operating room, say three mornings a week for a couple of months and observe. After this, he might be permitted to scrub up and act as second assistant at the operating table, an arrangement which would in no way interfere with the training of the intern or house resident acting as first assistant. After a month or so of getting the "feel," observing technic, and discussing findings and procedures with the operator, my surgeon friend felt that he would be justified in helping the young surgeon with a few cases of his own. A general practitioner in a rural community might come to the city, say once a week, for a longer period of instruction under such a plan. Also, the same small town doctor can make similar arrangements with an established general practitioner in his own community who has a good surgical training and has become established as a successful surgeon. Repeated postgraduate study in surgery each year will increase his efficiency.

So, we must send to the rural communities young doctors with adequate special training. We must train an ever-increasing number of men to do good general surgery, and we must train them for the particular needs of the communities in which they settle. We must urge the citizens of small communities and towns to build good, well-equipped hospitals, and it is our moral obligation to the public to see that these new hospitals and the new young doctors who move to these communities complement each other. In the cities we must lend a helping and instructing hand to these general practitioners who desire to improve their technic and surgical ability. These things we must do, if we are to meet successfully the mounting tide of bureaucratic interference and lay criticism, and if we are to survive as a profession of free men.

BIBLIOGRAPHY

1. Lehman, Edwin P.: J.A.M.A., **146**:279 (May 19) 1951.
2. Bibler, Lester D.: J.A.M.A., **147**:361 (Sept. 29) 1951.

DISCUSSION (*Abstract*)

Dr. William J. Fetzer, San Antonio, Tex.—No one doubts that we are living in a critical period, but I cannot help believing that the present crisis is largely due to the efforts of certain elements in our era, namely: the large farm organizations, powerful labor unions and our socialist government. But whether the crisis is a natural outgrowth of our evolution, or is being brought to a head by the planners, the fact remains we are in a crisis in medicine, which is only a part of the general challenge to our American way of living.

Fundamentally we must not lose sight of a generally accepted fact, and that is, the people of these United

States, as a whole, have been called the healthiest people on the earth . . . and that state of good health is due in large part to the results of good medical care administered by a profession interested primarily in the health of the individual.

I wish to call attention to a frequently overlooked fact, and that is, that the great burden and privilege of bringing good medical care to the people has been borne by the general practitioner, frequently unsung, overlooked and criticized. Only recently has this sleeping giant begun to awaken, and it is our national pride to acclaim the American Academy of General Practice which is bringing about the awakening.

But let us turn to the specific subject under discussion, and that is, surgical training for the general practitioner. In a handbook published in 1950, prepared by the Council on Medical Education and Hospitals of the American Medical Association, and entitled "Essentials of Approved Residencies and Fellowships" (page 40) it is recommended that graduates from medical school who intend to enter general practice spend one year of internship, which we assume is a rotating type, followed by a two-year residency. Only four months of surgery are recommended, and time is to be devoted to diagnosis, preoperative and postoperative care, minor surgery and emergency care.

Dr. L. B. Jackson, in San Antonio, saw the inadequacy as far as surgical training of this recommendation. He prepared a resolution suggesting that at least eight months out of the twenty-four be devoted to surgery, four of these to embrace operating room experience as assistants in major surgery. This resolution was passed unanimously by the Bexar County Academy of General Practice, by the House of Delegates of the Texas State Medical Association and, I understand, it was also passed by the House of Delegates of our parent organization, the American Medical Association and has been referred to the appropriate committee.

In closing, the author wishes to offer his recommendations for a solution to the problems of surgical training for the general practitioner.

First, a rotating internship of one year, for purposes of orientation.

Second, one to five years of actually doing general practice for further orientation and "finding himself."

Third, a careful, soul-searching examination of just what he really wants to do, with particular attention to the question, why do surgery and general practice? Is a large income desired, or does he wish to perform surgical procedures on his patients for the correction of conditions that are amenable only to surgery?

Fourth, if after the passage of a reasonable period of time of doing general practice under the above plan, the young physician has determined to further his surgical training and experience, he will be more mature, his judgments will be wiser, his knowledge will be greater of what is most needed by his particular type of practice, and he will be in a better position, both from the standpoint of maturity and economically, to choose the surgical training he needs in the many surgical centers, large and small, that are well able to give him what he requires.

THE COXSACKIE VIRUSES

PROPERTIES, IMMUNOLOGICAL ASPECTS AND ROLE IN HUMAN DISEASE*

By S. EDWARD SULKIN, Ph.D.
Dallas, Texas

During the last decade a large number of hitherto unrecognized viral agents have been discovered. In many cases these agents have been recognized as the cause of diseases which have been known for many years; in a few instances the recognition of an agent or group of agents has led to the discovery of a disease entity. The recently discovered "Coxsackie group of viruses," which has received a great deal of attention in the last five years, will be treated extensively in this review.

Following a small outbreak of poliomyelitis in upstate New York in August, 1947, Dalldorf and Sickles[1] reported the isolation of an unidentified filtrable agent from the feces of two patients with muscular weakness. The virus was distinct from that of poliomyelitis in that it could be isolated only by the inoculation of suckling mice or hamsters; monkeys were not susceptible. The lesions produced consisted of widespread degeneration of the skeletal muscles, without any apparent involvement of the central nervous system. Since the virus was recovered from patients with paralysis during a time when a small outbreak of poliomyelitis was occurring, it seemed important to learn something of the prevalence of this virus and its relation to poliomyelitis. The first confirmation and extension of the work of Dalldorf and his associates[1,2] was published by Melnick and his colleagues[3] in 1949 and soon an extensive literature began to accumulate. It is now evident that this new family of viral agents, designated provisionally the "Coxsackie group of viruses,"† is very widespread, and that certain serologic types may be found all over the world.[4] The Coxsackie viruses were in existence long before they were discovered by Dalldorf and his associates. The agent has been recovered from

*Read in Section on General Practice, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

*From the Department of Bacteriology, Southwestern Medical School of the University of Texas, Dallas, Texas.

†So named because the human cases from whom the virus was first isolated were residents of a village by that name in the upper Hudson River Valley, and because a number of viruses seem to be involved.

flies collected in 1943 and maintained in a dry ice storage cabinet for several years;[4] it has also been demonstrated by us in a number of stool specimens which had been stored under similar conditions for at least six years.

Classification of Coxsackie Viruses.—Very early in the investigations of these viral agents it became evident that numerous immunologic types existed, some with different tropisms for certain infant mouse tissues. There are also indications that the various serologic types differ to some extent in their pathogenic potentialities. On the basis of the lesions produced in infant mice Dalldorf[5] distinguished two groups of Coxsackie viruses (*Table 1*). Those falling in the more numerous group A category produce a rapidly progressive flaccid paralysis involving all the skeletal muscles but not the myocardium. The skeletal muscles show a diffuse degeneration which is followed by round cell infiltration and marked proliferation of sarcolemma nuclei. The muscle lesions although highly characteristic are not pathognomonic of C virus infection* Virus is present throughout the tissues and in the blood stream but is usually found in maximum concentration in the muscles. Although virus is present in the brain central nervous system lesions are minimal or absent. Muscular degeneration is less extensive and is usually focal in animals infected with C virus strains which fall in the group B category. However, severe degenerative necrotic lesions occur in the brain and frequently result in large areas of cystic degeneration. Baby mice infected with group B strains usually live longer than those infected with group A strains and develop tremors, ataxia and spasticity.

The Coxsackie viruses, then, produce in suckling mice a systemic disease involving many organ systems, the skeletal muscle being the tissue most constantly affected. Histopathologic studies reveal acute widespread degenerative lesions of the striated muscle, focal myocardial and generalized fat necrosis, hepatitis, pancreatitis and encephalomyelitis.[5–8]

Because of the accumulating evidence that the individual members of this group of viruses differ among themselves in a number of respects, it is apparent that we are dealing with a heterogeneous mixture of viral agents which requires further classification. In addition to differing among themselves serologically and in their pathogenesis in experimental animals, there is evidence of differences among group A and B strains in thermosusceptibility, effect of pH, and even in size.[12 20–24] There are indications, too, that certain C virus infections may have distinct epidemiologic patterns. All members of the C virus family, however, are highly resistant to the effects of physical and chemical agents. They withstand exposure to a wide range of pH (although some variations exist among different serologic types) and remain unaffected by a variety of agents including ether, penicillin, chloromycetin, streptomycin and a number of commonly used bactericidal agents. One stain of C virus (Dallas-M.B. strain) retained its activity after exposure to 0.5 per cent phenol at room temperature for at least one month.[25]

Host Range.—The host range for the C viruses is extremely narrow and appears to be limited to man and certain infant rodents (mice and hamsters). After serial passage in infant mice, animals up to about three weeks of age are susceptible to certain strains of C virus, but there is evidence that this may be related to the concentration of virus used in the inoculum. Attempts to adapt certain strains to older mice

*It is clearly evident now that neither Group A or B strains of C virus are related to other viruses which induce similar lesions in striated muscle.

SEROLOGIC TYPES OF COXSACKIE VIRUSES*

Group†	Type	Prototype Strain Identification	Place of Origin	Strains from Other Laboratories
	1	T.T.	New York State	Easton-2 (Pennsylvania)[9]
	2	Fl.	Wilmington, Del.	
	3	J.Ol.	New York State	
	4	Howitt[10]		Minnesota Sy-1, Sy-2[11] Texas-1, High Point[12] Dallas-M.B.[13]
A	5	Howitt[10]		
	6	C.G.	New York State	
	7	W.P.	New York State	
	8	C.D.	New York State	
	9	P.B.	New York State	
	10	N.K.	New York State	
	1	P.O.	New York State	Conn.-5[14]
B	2	Ohio-R[15]	Cincinnati, Ohio	
	3	Nancy[16]	New Haven, Conn.	Hoquiam, Wash.[17]

*Serologic classification provided through the courtesy of Dr. Gilbert Dalldorf, Director, Division of Laboratories and Research, New York State Department of Health, Albany.

†Not including the Group A immunologic types of "H" virus isolated from patients with herpangina,[18] nor the agent isolated from North Alaskan Eskimos.[19]

TABLE 1

by alternate passage through suckling and weaned mice, have resulted in failure.[25 26] The lack of susceptibility of mature mice and hamsters, however, may not be regarded as a distinguishing characteristic for all types of Coxsackie viruses because at least one strain (group B, Conn.—5) has been passed in adult mice with the production of pancreatic disease.[27] Using the same strain, Kilbourne and Horsfall[28] have shown that adult mice may be lethally infected if cortisone (Merck, 11-dehydro-17-hydroxycorticosterone-21-acetate) is administered prior to the inoculation of virus. These observations have now been extended to include a number of serologic types of Coxsackie viruses.[20]

Although monkeys do not develop overt infection following parenteral inoculation of virus,[2 12] Melnick and Ledinko[29] showed that following oral administration of virus an infectious state may be established in cynomologous monkeys but not in rhesus or cercopithecus (green) monkeys. The animals develop a febrile response with no evidence of muscle or central nervous system lesions and become pharyngeal and intestinal carriers. Both neutralizing and complement-fixing antibodies are produced. Following oral administration of virus a similar response occurs in chimpanzees. The animals exhibit immunity to homologous strains lasting at least one year, and neutralizing antibodies specific for the strain used in producing the infection are demonstrable. Although rises in complement-fixing antibody titers usually occur after the feeding of different viruses, antibodies to heterologous types are occasionally demonstrable at the same time suggesting an anamnestic response.

Newborn guinea pigs are refractory to C virus infection and in limited attempts Dalldorf and his associates[2] and Melnick[12] found the agent to be nonpathogenic for fertile hens' eggs. Huebner and his co-workers,[30] however, succeeded in adapting one serologic type (group A, type 2) to chick embryos using the technic of alternating mouse-to-egg passage. These observations have been confirmed in our laboratory and attempts are being made to adapt other serologic types of C virus to developing chick embryos.[25] Slater and Syverton[11] succeeded in propagating a strain of C virus (group A, type 4 Minnesota strain) *in vitro* in the presence of minced embryonic mouse cells and Simm's UF/3x7 fluid.

Clinical Aspects.—Although much information exists regarding the properties of the members of the Coxsackie group of viruses, little is actually known about the disease or diseases which they produce. The repeated isolation of C viruses in widely scattered areas, both from ill and well persons,[31 32] together with the widespread occurrence of antibodies to numerous serologic types,[12] suggests that this family of viruses is widely prevalent in nature. Since these agents may also occur indiscriminately among seriously ill persons this causal relationship to certain clinical entities must be evaluated cautiously. It is already evident that infection of man with these agents may result in diverse clinical manifestations.[2 14 33] Because the prototype strains were isolated from patients who presented the clinical picture of poliomyelitis it was felt originally that these agents might be in some way associated with poliomyelitis. The Coxsackie viruses have been found repeatedly in close association with poliomyelitis during epidemics of the latter disease but their pathogenicity here remains to be elucidated.[31 32 34] That the C virus may be significant in some of the non-paralytic cases of "poliomyelitis" is suggested by the epidemiologic observations of Curnen and others.[14 32] The observation that late summer outbreaks of so-called poliomyelitis may be mixed epidemics is highly significant since both Coxsackie and poliomyelitis viruses are known to be prevalent during that season. When reliable diagnostic aids are developed it will no doubt be possible to identify some of the cases of so-called "abortive poliomyelitis" as C virus infections.

Despite the earlier observations associating the C viruses with poliomyelitis and poliomyelitic-like infections, there is increasing evidence that certain strains may produce a varied clinical pattern. Kilbourne,[33] for example, describes a small outbreak attributable to these agents in which such divergent clinical entities as acute appendicitis, sinusitis, infectious mononucleosis, pleurodynia and influenza were involved. Coxsackie viruses have now been isolated from clinical syndromes resembling paralytic and non-paralytic poliomyelitis, aseptic meningitis, pleurodynia, a number of minor illnesses including summer grippe, three-day fever, influenza-like illnesses, and more recently herpangina, a specific clinical entity of children. The evidence that the C virus may be associated with these

syndromes is based on a number of laboratory infections,[32] a single known experimental infection,[35] occasional sporadic clinical infections,[3 12 13] and a few small epidemics.[17 18 33 36 37] Most investigators who have studied these infections suggest a causal relationship between the viral agent and the disease produced. Because these agents have been isolated from both ill and well persons,[31 32] as pointed out previously, it is difficult to evaluate some of these observations. However, the evidence associating members of this family with vesicular pharyngitis (herpangina)[18 31] and epidemic pleurodynia (Bornholm disease or "devil's grippe")[35 36 37] is more impressive. The first reference to the causal relationship between a Coxsackie virus and a patient with characteristic symptoms of pleurodynia, a disease well known to physicians, was made by Curnen.[36] Since then this relationship has been confirmed by other investigators.[17 25 35 37] The etiological relationship of the C virus to herpangina, a specific clinical entity of children originally described by Zahorsky,[38] and apparently not familiar to many physicians, was recently pointed out by Huebner and his associates.[18 31] It is suggested by these investigators on the basis of the demonstration of several types of similar viruses in persons with this disease, that herpangina may represent the chief clinical manifestation of human infection with the group A Coxsackie viruses. These observations must await confirmation although they appear to be both epidemiologically and statistically significant.

Diagnosis.—A definitive diagnosis of C virus infection in man can be made only by laboratory methods, and even when adequate available procedures are employed concurrent infection with the poliomyelitis virus or some other agent must be excluded. The C viruses have been recovered from the feces or throat washings of patients, persons recently ill or in close contact with a sick person, and occasionally well persons. Some reports indicate that these agents may be recovered from cerebrospinal fluid or from the blood stream, but this is generally not the case. The procedure usually employed consists of the inoculation of the specimen, previously treated to remove contaminating micro-organisms, into immature mice. At least two litters of suckling mice are recommended for each specimen.[39] Animals are examined for evidence of infection during an observation period of at least two weeks. In man as well as in experimental animals C viruses stimulate the production of type-specific neutralizing and complement-fixing antibodies which are used in the identifications of virus strains and in establishing a serologic response to infection. Although the recovery of a C virus and the demonstration of an increase in antibody response to the homologous type is good evidence of causal relationship to the disease condition being investigated, there is evidence that increases in serum antibody levels may occur in apparently healthy persons from whom virus is isolated.[40] The neutralization test widely used in the study of virus disease is being used by a number of investigators in the study of C virus infection in man. A detailed account of the technic and application of the test is presented by Melnick and Ledinko.[16] Melnick and his associates[41] have suggested the use of litters born to immune mothers as a means of typing strains of C virus. However, the procedure seems to be feasible only when large numbers of mature mice are undergoing immunization to known types of virus.

Several workers have investigated the possible application of the complement fixation test as a diagnostic method in man as well as a means of typing strains of C virus.[10 42 43 44] Although the multiplicity of serologic types of C virus is a serious drawback to the use of such tests as a means of diagnosis, attempts are being made to improve antigens for use in a standard complement fixation test. There are indications that various types of C virus can be mixed to prepare polyvalent antigens that will give positive complement fixation tests with sera containing antibodies to each of the types of C virus contained in the antigen.[25] Studies have already indicated that such polyvalent complement-fixing antigens can be used with experimentally produced hyperimmune sera and with certain human sera. Efforts are now being directed toward improving and evaluating such systems for practical use in the clinical laboratory.

Complicating the use of serologic tests in the diagnosis of disease caused by this group of agents is the fact that C virus antibodies are usually detectable very early in the course of the illness. Consequently, in order to demonstrate unequivocally a specific rise in antibody response during the illness it is necessary that specimens be obtained soon after the onset of the illness as well as during convalescence. Further com-

plicating the use of serologic tests is the fact that C virus antibodies are demonstrable in the serum of a considerable number of healthy persons.[3 40 44 45] It is obvious, then, that presence of specific C virus antibodies has little or no diagnostic value so far as current illness is concerned unless a specific rise in titer can be demonstrated as the disease progresses.

BIBLIOGRAPHY

1. Dalldorf, Gilbert; and Sickles, G. M.: An Unidentified, Filtrable Agent Isolated from the Feces of Children with Paralysis. Science, **108**:61, 1948.
2. Dalldorf, Gilbert; Sickles, G. M.; Plager, H.; and Gifford, Rebecca: A Virus Recovered from the Feces of "Poliomyelitis" Patients Pathogenic for Suckling Mice. J. Exper. Med., **89**:567, 1949.
3. Melnick, J. L.; Shaw, Ernest W.; and Curnen, E. C.: A Virus Isolated from Patients Diagnosed as Nonparalytic Poliomyelitis or Aseptic Meningitis. Proc. Soc. Exper. Biol. & Med., **71**:344, 1949.
4. Melnick, Joseph L.: Part V—The Poliomyelitis, Encephalomyocarditis, and Coxsackie Groups of Viruses (Symposium on Viral and Rickettsial Diseases). Bact. Rev., **14**:233, 1950.
5. Dalldorf, Gilbert: The Coxsackie Viruses. Bull., N. Y. Acad. Med., **26**:329, 1950.
6. Pappenheimer, Alwin M.; Daniels, J. B.; Cheever, F. S.; and Weller, T. H.: Lesions Caused in Suckling Mice by Certain Viruses Isolated from Cases of So-called Nonparalytic Poliomyelitis and of Pleurodynia. J. Exper. Med., **92**:169, 1950.
7. Melnick, Joseph L.; and Godman, Gabriel: Pathogenesis of Coxsackie Virus Infection. Multiplication of Virus and Evolution of the Muscle Lesion in Mice. J. Exper. Med., **93**:247, 1951.
8. Gifford, R.; and Dalldorf, G.: The Morbid Anatomy of Experimental Coxsackie Virus Infection. Amer. J. Path., **27**:1047 (Nov.) 1951.
9. Melnick, J. L.; and Kaplan, A. S.: Dual Antibody Response to Coxsackie and Poliomyelitis Viruses in Patients with Paralytic Poliomyelitis. Proc. Soc. Exper. Biol. and Med., **74**:812, 1950.
10. Howitt, Beatrice F.; and Benefield, Ursula R.: Use of Complement Fixation in the Differentiation of Strains of Coxsackie Virus. Proc. Soc. Exper. Biol. and Med., **73**:90, 1950.
11. Slater, Eben A.; and Syverton, J. T.: The Cultivation of Coxsackie Virus. Proc. Soc. Exper. Biol. & Med., **74**:509, 1950.
12. Melnick, Joseph L.: Studies on the Coxsackie Viruses: Properties, Immunological Aspects and Distribution in Nature. Bull. N. Y. Acad. Med., **26**:342-356 (May) 1950.
13. Sulkin, S. E.; Manire, G. P.; and Farmer, Thomas W.: Cross-Neutralization Tests with Coxsackie Viruses. Proc. Soc. Exper. Biol. & Med., **73**:340, 1950.
14. Curnen, E. C.; Shaw, E. W.; and Melnick, J. L.: Disease Resembling Nonparalytic Poliomyelitis Associated with a Virus Pathogenic for Infant Mice. J.A.M.A., **141**:894, 1949.
15. Melnick, J. L.; Ledinko, N.; Kaplan, A. S.; and Kraft, L. M.: Ohio Strains of Virus Pathogenic for Infant Mice (Coxsackie group). Simultaneous Occurrence with Poliomyelitis Virus in Patients with "Summer Grippe." J. Exper. Med., **91**:185, 1950.
16. Melnick, J. L.; and Ledinko, Nada: Immunological Reactions of the Coxsackie Viruses. The Neutralization Test: Technic and Application. J. Exper. Med., **92**:463, 1950.
17. Lazarus, Alfred S.; Johnston, Elizabeth A.; and Galbraith, James E.: An Outbreak of Epidemic Pleurodynia with Special Reference to the Laboratory Diagnosis of Coxsackie Virus Infections. Amer. J. of Pub. Health, **42**:20, 1952.
18. Huebner, R. J.; Cole, Roger M.; Beeman, Edward A.; Bell, Joseph A.; and Peers, James H.: Herpangina. Etiological Studies of a Specific Infectious Disease. J.A.M.A., **145**:628, 1951.
19. Banker, D. D.; and Melnick, J. L.: Isolation of Coxsackie Virus from North Alaskan Eskimos. Amer. J. Hyg., **54**:383, 1951.
20. Sulkin, S. E.; Wallis, C.; and Donaldson, P.: Influence of Cortisone, Route of Inoculation and Age on Susceptibility of Mice to Coxsackie Viruses. To be published.
21. Quigley, J. J.: Ultrafiltration and Ultracentrifugation Studies on Coxsackie Virus. Proc. Soc. Exper. Biol.. & Med., **72**:434, 1949.
22. Melnick, J. L.; Rhian, Morris; Warren, Joel; and Breese, S. S., Jr.: The Size of Coxsackie Viruses and Lansing Poliomyelitis Virus Determined by Sedimentation and Ultrafiltration. J. Immunol., **67**:151, 1951.
23. Himmelweit, F.; Findlay, G. M.; and Howard, E. M.: The Size of Coxsackie Viruses as Estimated by Filtration Through Gradocol Membranes. Brit. J. Exper. Path., **31**:809, 1950.
24. Robinson, Lucena K.: Effect of Heat and of pH on Strains of Coxsackie Virus. Proc. Soc. Exper. Biol. & Med., **75**:580, 1950.
25. Unpublished observations.
26. Gifford, Rebecca; and Dalldorf, G.: Creatine, Potassium, and Virus Content of the Muscles Following Infection with the "Coxsackie Virus." Proc. Soc. Exper. Biol. and Med., **71**:589, 1949.
27. Pappenheimer, A.; Kunz, L.; and Richardson, S.: Passage of Coxsackie Virus (Conn.-5 Strain) in Adult Mice with Production of Pancreatic Disease. J. Exper. Med., **94**:45, 1951.
28. Kilbourne, E. D.; and Horsfall, F. L., Jr.: Lethal Infection with Coxsackie Virus of Adult Mice Given Cortisone. Proc. Soc. Exper. Biol. and Med., **77**:135, 1951.
29. Melnick, J. L.; and Ledinko, N.: Infection of Cynomologus Monkeys with the Ohio Type of Coxsackie Virus (C Virus). J. Immunol., **64**:101, 1950.
30. Huebner, R. J.; Ransom, S. E.; and Beeman, E. A.: Studies of Coxsackie Virus Adaptation of a Strain to Chick Embryos. Pub. Health Rep., **65**:803, 1950.
31. Cole, Roger M.; Bell, J. A.; Beeman, Edward A.; and Huebner, Robert J.: Studies of Coxsackie Viruses: Observations on Epidemiological Aspects of Group A Viruses. Amer. J. of Pub. Health, **41**:1342, 1951.
32. Sulkin, S. E., *et alii*: Dual Infection with Poliomyelitis and Coxsackie Viruses in Contacts of Poliomyelitis Patients and in Presumably Normal Persons. To be published.
33. Kilbourne, Edwin D.: Diverse Manifestations of Infection with a Strain of Coxsackie Virus. Fed. Proc., **9**:581, 1950.
34. Melnick, Joseph L.; Kaplan, Albert S.; Zabin, Eva; Contreras, Guillermo; and Larkum, Newton W.: An Epidemic of Paralytic Poliomyelitis Characterized by Dual Infections with Poliomyelitis and Coxsackie Viruses. J. Exper. Med., **94**:471, 1951.
35. Findlay, G. M.; and Howard, Elsie M.: Coxsackie Viruses and Bornholm Disease. Brit. Med. J., **1**:1233, 1950.
36. Curnen, Edward C.: Human Disease Associated with the Coxsackie Viruses. Bull. N. Y. Acad. Med., **26**:335, 1950.
37. Weller, T. H.; Enders, J. F.; Buckingham, M.; and Finn, J. J., Jr.: The Etiology of Epidemic Pleurodynia: A Study of Two Viruses Isolated from a Typical Outbreak. J. Immun., **65**:337, 1950.
38. Zahorsky, J.: Herpetic Sore Throat. Sou. Med. J., **13**:871, 1920.
39. Sulkin, S. Edward; Schwab, M.; and Wallis, H. C.: Litter Differences Among Suckling Mice. Proc. Soc. Exper. Biol. and Med., **77**:354, 1951.
40. Huebner, Robert J.; Armstrong, C.; Beeman, E. A.; and Cole, R. M.: Studies of Coxsackie Viruses. J.A.M.A., **144**: 609, 1950.
41. Melnick, J. L.; Clarke, N. A.; and Kraft, Lisbeth M.: Immunological Reactions of the Coxsackie Viruses. III. Cross-Protection Test in Infant Mice Born of Vaccinated Mothers. Transfer of Immunity Through the Milk. J. Exper. Med., **92**:499-505, 1950.
42. Manire, G. P.; Sulkin, S. E.; and Farmer, Thomas W.: Complement Fixation with a Coxsackie Virus. Proc. Soc. Exper. Biol. and Med., **73**:341, 1950.
43. Kraft, Lisbeth M.; and Melnick, Joseph L.: Immunological Reactions of the Coxsackie Viruses. II. The Complement Fixation Test. J. Exper. Med., **92**:483, 1950.
44. Olitsky, P. K.; Casals, J.; and Murphy, L. C.: Diagnostic Tests with Albany Type I and II Coxsackie (Dalldorf) Virus. Fed. Proc., **9**:388, 1950.
45. Manire, G. P.; Sulkin, S. E.; and Farmer, T. W.: Complement-Fixing and Neutralizing Antibodies for a Coxsackie Virus in Sera from Suspected Patients and Normal Persons. Bacteriological Proc. Annual Meeting. Soc. American Bact., Baltimore, Md., p. 82, 1950.

DISCUSSION (*Abstract*)

Dr. Thomas W. Farmer, Dallas, Tex.—It now appears most likely that the Coxsackie viruses are related to herpangina and possibly to epidemic pleurodynia. There is no clear-cut evidence that they are responsible for paralytic diseases in man.

Dr. Robert E. Blount, Fort Sam Houston, Tex.—The identification of the Coxsackie virus and its probable relation to central nervous system infections certainly narrows down the large and puzzling field of the "aseptic meningitides." Another successful attack on this group of "aseptic meningitis" cases was made when Dr. Paul

Beeson of Emory proved that *Leptospira pomona* infections could cause such a picture. Two years ago on Okinawa we had an outbreak of aseptic meningitis among soldiers who had been swimming in an "off limits" fresh water pool in a coral quarry. Twenty men developed a clinical picture of "aseptic meningitis." This was characterized by headache, vomiting, nuchal rigidity, conjunctival suffusion and cerebrospinal fluid pleocytosis. Only two men had questionable residual muscle weakness. We had mentally ruled out leptospirosis because of the lack of jaundice. Recently Dr. Ross Gauld of the virus laboratories of the Walter Reed Army Medical Center, on reviewing these cases, had agglutination tests of *Leptospira icterohemorrhagiae, L. pomona,* and *L. hebdomadis* run on the serum from one of the cases (we had saved serial sera from all these cases). Not only did that one case prove positive, but all twenty, for *Leptospira hebdomadis* which causes a disease in Japan known as three-day fever (Gauld *et alii,* unpublished data).

While on leave in July, 1951, in Bassfield, Mississippi, I observed what appeared clinically to be a typical outbreak of herpangina. A number of children four to seven years of age developed an illness of brief duration, characterized by fever, sore throat, and the appearance of small vesicles over the nasopharynx and soft palate, each surrounded by a small red halo.

RESPIRATORY ACIDOSIS AND ALKALOSIS*

By FONTAINE S. HILL, M.D.
Memphis, Tennessee

Disturbances of fluid and electrolyte balance continually confront the clinician in many diseases seen commonly in pediatric practice. The changes which these disorders produce may account for many of the symptoms which the patient exhibits. Especially is this true in infants and children, who not only demonstrate a relatively greater daily obligatory water exchange than adults, but are more subject to such disturbances as vomiting and diarrhea, which easily distort acid-base relationships.

Metabolic derangements associated with disease processes and frequently observed in diabetes mellitus, chronic nephritis, pyloric obstruction and diarrheal diseases are usually well recognized. However, alterations in electrolyte structure based primarily on respiratory dysfunction are less common, and, therefore, too often go undetected. Difficulty in recognition of respiratory acidosis and alkalosis is enhanced by the fact that the signs and symptoms presented by these conditions may simulate those present in the opposite metabolic disorder. For example, hyperpnea causing respiratory alkalosis might easily be confused with compensatory Kussmaul breathing of metabolic acidosis. In addition, diagnosis of respiratory acidosis and alkalosis is dependent on measure of both plasma carbon dioxide combining power or alkali reserve and plasma pH. The latter is not always readily available.

The incidence of these derangements warrants a presentation of the basic mechanisms involved, their application to clinical cases, and therapeutic measures necessary to restore normal electrolyte patterns.

Any alteration in the ability of the lungs to eliminate carbon dioxide properly will produce respiratory acidosis or alkalosis. Since the respiratory mechanism is largely responsible for prevention of wide variations in plasma pH, one would expect rise or fall of pH to occur early in conditions causing inadequate pulmonary function. This is in contrast to metabolic disturbances of acid-base relationships which are characterized by deviations of alkali reserve prior to alterations in plasma pH.

RESPIRATORY ACIDOSIS

The underlying abnormality in respiratory acidosis is an increase in blood carbonic acid, which follows elevation of carbon dioxide in the pulmonary alveoli.[1,2] This may result from: (1) breathing air containing abnormally high percentages of carbon dioxide; and (2) conditions in which elimination of carbon dioxide through the lungs is retarded. This group includes: bronchopneumonia; cardiac decompensation, in which pulmonary congestion and slowed circulation combine to produce increased carbon dioxide tension in the blood; pulmonary emphysema, especially that resulting from severe bronchiolitis and asthma; morphine narcosis; poliomyelitis, in which alveolar ventilation may be reduced; convulsive apnea; pulmonary fibrosis accompanying cystic disease of the pancreas; and laryngeal obstruction, as observed in acute laryngotracheobronchitis. Pulmonary edema caused by toxic irritants or infection may also be included.

---

*Read in Section on Pediatrics, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

*From the Pediatric Division, College of Medicine, University of Tennessee and the John Gaston Hospital, Memphis, Tennessee.

The following case of fibrocystic disease of the pancreas illustrates the changes in acid-base relationships which may occur with pulmonary obstruction.

C. K., an eleven months old white male, had experienced frequent wheezing and coughing since one month of age. Severe tracheobronchitis had occurred when the infant was five months old. Wheezing and coughing continued intermittently, and the patient was admitted to the hospital because of cyanosis, fever, vomiting, and diarrhea of moderate degree. Dehydration was also present. The vomiting and diarrhea ceased after several days and cyanosis and severe dyspnea dominated the clinical picture. Twelve days after admission the plasma pH was 7.04 and the carbon dioxide combining power 83 volumes per cent. Stool examinations were negative for trypsin activity. The urine pH was consistently acid. Daily water and salt requirements were met but the patient was discharged one month later unimproved.

A brief review of the normal acid-base composition of blood plasma will be helpful in clarification of changes which occurred in this case of respiratory acidosis.

Failure to understand the mechanisms involved in respiratory acidosis and alkalosis stems chiefly from the reigning confusion regarding terminology. Although the terms respiratory acidosis and alkalosis are in common usage, they lend themselves to much misunderstanding. The confusion rests in use of the term acidosis to mean both lowered pH and lowered alkali reserve, and alkalosis to have the opposite meanings. In so-called respiratory acidosis, there is an excess of blood carbonic acid which results in a lowered plasma pH or acidemia. To restore the normal pH, an increase in alkali reserve or alkalosis must ensue. Nowhere does an acidosis supervene if the sequence of events goes undisturbed. Respiratory alkalosis actually consists of a series of electrolyte changes characterized by an initial alkalemia or increased pH compensated by acidosis or lowered alkali reserve. Likewise, alkalosis, taken to mean an elevated alkali reserve, does not occur. However, for conventional reasons, the commonly used terms have been employed while keeping the more correct terminology in mind.

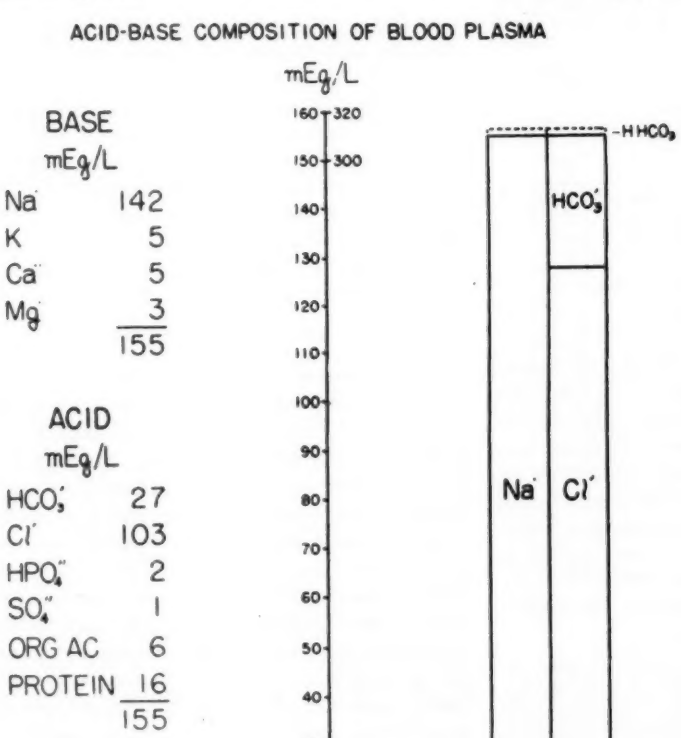


CHART 1

Normal acid-base composition of blood plasma. (Gamble,[3] illustration used by permission.)

Chart 1, which was devised by Gamble,[3] illustrates the relationship of the acid-base components of the blood plasma and their concentrations in the plasma. It will be noted that basic ions are on the left and acid ions on the right, and that with this arrangement the relative quantities of the various components are easily visualized. Sodium comprises 91 per cent of the base and chloride 66 per cent of the

total acid radicles. The bicarbonate ion (HCO_3) is the next largest item of the acid side and is determined by the amount of base available after all other acid radicles have been balanced.

In health, the reaction of the blood remains within the range of pH 7.30 and 7.45, and, because of exceedingly efficient buffer mechanisms, there may be little or no change from normal even in disease states. Of the various buffer systems in the blood, the free carbonic acid-base bicarbonate ($H.HCO_3$:$B.HCO_3$) buffer is one of the most important. The ratio of $H.HCO_3$:$B.HCO_3$ is normally 1:20. At this ratio the pH of blood plasma remains within normal limits. Carbonic acid ($H.HCO_3$) has a normal value of 3 volumes per cent or 1.35 mEq. per liter and bicarbonate covering base ($B.HCO_3$) is normally 60 volumes per cent or 27 mEq. per liter. Carbonic acid and thus bicarbonate is directly under control of the respiratory mechanism and with this exception all plasma components are largely regulated by renal function. The method of maintaining plasma protein levels is unknown. The sum of carbonic acid and base bicarbonate is the total plasma carbon dioxide content whereas the carbon dioxide combining power represents only bicarbonate covering base. Therefore, measure of the latter indicates the reserve of base readily available for the neutralization of all acids stronger than $H.HCO_3$ and is synonymous with alkali reserve.[4] Acidosis exists when the alkali reserve is decreased and alkalosis has the opposite meaning of increased alkali reserve.

Variations in pH are evidenced clinically by changes in rate and depth of respirations, since the blood carbonic acid concentration depends ultimately on elimination of carbon dioxide from the body by the lungs.

Carbon dioxide tension in the blood is increased in any condition obstructing escape of carbon dioxide from the alveoli. Rise in blood $H.HCO_3$ follows with decrease in plasma pH. Therefore, there is an uncompensated primary carbonic acid excess. To compensate for this and thus restore pH to normal range, $B.HCO_3$ must also be increased. For correction of these alterations, the body brings into play certain compensatory mechanisms which not only tend to maintain normal pH but also account for the various clinical and laboratory findings of respiratory acidosis. These mechanisms are as follows:[2] (1) Increased ventilation. This results from stimulation of the respiratory center by excessive carbon dioxide in the blood with consequent increase in rate and depth of respiration. Although the respiratory center is sensitive to only slight change in carbon dioxide tension, depressed breathing may dominate the picture if respiratory paralysis or narcosis is the underlying factor. Therefore, labored breathing might be observed in one patient with respiratory acidosis and depressed respirations in another, depending on the pathologic process at play. The clinician might easily confuse the former with hyperpnea of metabolic acidosis and the latter with apnea of metabolic alkalosis, unless determination of both alkali reserve and plasma pH are obtained. Metabolic acidosis produces both a lowered pH and alkali reserve, whereas the two values are elevated in metabolic alkalosis. Respiratory acidosis eventuates in an elevation of alkali reserve as compensation for an initial decrease in plasma pH. (2) Increase in alkali reserve. This is made possible by increased renal excretion of chloride which permits accumulation of $B.HCO_3$ and return of the $H.HCO_3$:$B.HCO_3$ ratio to normal range. Therefore, hypochloremia and initial acid reaction of the urine occur. (3) Increased ammonia formation. The kidneys produce and excrete ammonia at increased rate, thereby diminishing loss of base from the body with consequent conservation of alkali reserve. (4) Increased urine acidity. Acid radicles other than chloride are eliminated in the urine to allow extension of alkali reserve.

From consideration of the foregoing compensatory mechanisms, one would expect the following laboratory findings in respiratory acidosis: (1) pH below normal range; (2) increased carbon dioxide combining power or alkali reserve; (3) lowered blood chlorides; (4) acid urine reaction.

Therapy of respiratory acidosis would include the following:[1] (1) Artificial respiration, oxygen, and respiratory stimulants to overcome asphyxia and respiratory paralysis; (2) Early relief of obstruction in the air passages which prevents escape of carbon dioxide. These measures might include tracheotomy, bronchoscopic suction, bronchial dilator drugs, expectorants with the exception of ammonium chloride, an acid-forming salt, and placing the patient in an atmosphere of increased humidity to render the bronchial secretions less viscid. Relief of bronchial ob-

struction in fibrocystic disease of the pancreas is most difficult to achieve because of the continuous formation of viscid bronchial secretions, a basic abnormality in this condition. (3) Adequate hydration of the patient. Fluids containing salt are contraindicated, except in amounts necessary to meet daily sodium chloride requirements, since such fluids would interfere with the attempt of the kidney to lower plasma chloride and thereby permit increase of $B.HCO_3$.

That uncomplicated respiratory acidosis is not always present clinically is demonstrated by the following case:

A three-months-old white girl was admitted to the Children's Hospital with a clinical picture of acute bronchiolitis characterized by emphysema and severe dyspnea. Determination of pH was not done, but the carbon dioxide combining power was 24 volumes per cent. Urinalysis revealed one plus albuminuria. In view of bronchiolitis, respiratory acidosis would be expected with an elevated carbon dioxide combining power. It was apparent that uncomplicated respiratory acidosis did not exist since the alkali reserve was not increased. The patient expired on the fourth hospital day, and post-mortem examination revealed bilateral polycystic kidneys, in addition to the pulmonary pathology. Inability of the kidneys to excrete acid metabolites adequately and make ammonia prevented extension of the alkali reserve as compensation for increased blood carbonic acid.

RESPIRATORY ALKALOSIS

Respiratory alkalosis may result from any condition in which hyperventilation occurs as a primary manifestation.[1] Clinically, it is observed in salicylate poisoning, meningitis, encephalitis, and hyperpyrexic states, all of which may exhibit overbreathing due to stimulation of the respiratory center.[1] Other causes are hysteria, in which the disturbance is usually transitory, and high altitudes, where low atmospheric oxygen tension necessitates hyperventilation.[2] Regardless of etiology, the basic derangement is reduction of alveolar carbon dioxide tension followed by decrease in blood $H.HCO_3$. Therefore, plasma pH is raised, unless $B.HCO_3$ is reduced proportionately. The latter is accomplished by the following mechanisms:[2] (1) Excretion of alkali. Alkali in the form of bicarbonate is excreted in the urine early and in small degree unless other changes such as ketosis cause continued excretion. (2) Decreased acid elimination. (3) Retention of acid metabolic products. Ketone bodies accumulate in the blood and ketonuria may occur. (4) Retention of chlorides. Blood chlorides are maintained at normal or raised levels. (5) Decreased ammonia formation. This enhances elimination of base.

Since poisoning by salicylates is commonly encountered in pediatrics, emphasis will be given to derangements which occur following excessive absorption of these substances and measures necessary to restore electrolyte balance.

The following case report demonstrates the severe acidosis characteristic of salicylate poisoning in infants and young children, who apparently are more easily poisoned than older children and adults.[5]

A 2-year-old white boy was admitted to the Children's Hospital with the complaints of deep and rapid respirations, vomiting, and coma. The history revealed that the child had ingested a large but undetermined amount of aspirin 14 hours before admission. Three hours later he began to vomit and have hyperpnea. The latter was a prominent finding until clinical improvement was effected by intense therapy. On admission the carbon dioxide combining power was 10 volumes per cent and plasma pH 7.03. Urine pH was 5.5 and acetonuria was present. One-sixth molar sodium lactate followed by glucose solution was administered. Seven hours later the carbon dioxide combining power was 20 volumes per cent and plasma pH 7.29. Large amounts of lactate and glucose were given until laboratory findings were normal and the patient was free of symptoms. He was discharged on the fifth hospital day.

The first symptom of salicylate poisoning is hyperventilation which produces primary carbon dioxide deficit. Blood $H.HCO_3$ is reduced, thereby raising plasma pH. The aforementioned compensatory mechanisms come into play, especially urinary excretion of $B.HCO_3$, in an attempt to restore normal pH. Severe and persistent ketosis develops due to disturbance of glucose and glycogen metabolism which results from presence of salicylates. Therefore, acidosis ensues and mild acidemia may appear as reduction of B.HCO3 continues. Hyperpnea continues and tends to remain a prominent finding. This prevents extreme fall of plasma pH.[5] It is apparent that a sequence of events occurs which is first characterized by an increased plasma pH and lowered alkali reserve and later by decrease of both pH and alkali reserve if poisoning is of severe degree. Although the former electrolyte changes may result from mild intoxication, experience with patients on the pediatric wards of the John Gaston Hospital has emphasized the need for intense and vigorous administration of alkali for correction of severe acidosis. Sodium lactate is the alkali of choice because of its antiketogenic effect.[5] In addition, large amounts of glucose are required to abolish ketosis and must

be given until all salicylate has left the body. In those cases exhibiting alkalemia and acidosis, chloride-containing solutions are indicated to help restore pH to normal range by further decreasing alkali reserve.

In all cases of respiratory alkalosis there is danger of tetany although definite clinical manifestations are not commonly seen.[5] However, in those due to causes other than salicylate intoxication, a mixture of 30 per cent carbon dioxide and 70 per cent oxygen should be adminstered as quickly as possible to prevent extreme alkalemia with resultant hypocalcemia. This is more effective than drugs which prevent excessive elimination of carbon dioxide by depressing respiration but is usually of no avail in salicylate poisoning because hyperpnea due to central respiratory stimulation is usually transitory and the presenting problem is soon that of severe acidosis.

SUMMARY AND CONCLUSIONS

Respiratory acidosis and alkalosis are discussed with reference to basic mechanisms involved, etiology and therapy.

Case reports are presented to demonstrate how these problems confront the clinician.

REFERENCES

1. Spector, S.; and McKhann, C. F.: Respiratory Acidosis and Alkalosis in Children. J. Pediat., **32**:227, 1948.
2. Cantarow, A.; and Trumper, M.: Clinical Biochemistry. Philadelphia: W. B. Saunders Company, 1949.
3. Gamble, J. L.: Chemical Anatomy, Physiology and Pathology of Extracellular Fluid. Cambridge: Harvard University Press, 1950.
4. Best, C. H.; and Taylor, N. B.: The Physiological Basis of Medical Practice. Baltimore: The Williams and Wilkins Company, 1945.
5. Hartmann, A. F.: Acidosis and Alkalosis. Pediatrics, **2**:584, 1948.

PROLONGED VOMITING AS A CAUSE OF POTASSIUM DEFICIENCY*

By BURTON A. SHATZ, M.D.
and
FRANK J. CATANZARO, M.D.
St. Louis, Missouri

The alterations in the chemistry of the blood during intestinal obstruction and vomiting have been studied by many workers since the early 1900's.[1] Despite this fact, potassium disturbances have until recently been neglected, apparently because of the technical difficulties involved in the determination of potassium in the blood. It was not until 1937 that Scudder[2] reported marked hyperkalemia following experimental intestinal obstruction in cats. In the same year Cutler[3] reported similar findings in experiments performed on dogs. Cutler further observed that injection of potassium chloride intravenously in dogs caused sudden death. In contrast to these experimental findings, Falconer[4] in 1939 published a thorough study of potassium disturbances in 27 patients with intestinal obstruction. In no instance did he observe hyperpotassemia. On the contrary, his data showed that there is a definite tendency for the concentration of serum potassium to decrease during intestinal obstruction in man, and he was the first to give parenteral potassium with beneficial effect. Since that time, there have been numerous reports verifying his observations.

Because the conventional method of potassium determination was too difficult for routine hospital use, Falconer's important findings had little effect on the way the majority of clinicians handled their cases of intestinal obstruction. It was not until the development of the flame photometer, that a rapid method of determining serum potassium was made available. Since the introduction of this instrument, the detection and treatment of potassium disturbances have been greatly facilitated.*

According to Hoffman[6] the total body content of potassium in an adult is somewhat more than 160 grams. Only about three grams are contained in the extracellular fluid, the rest residing in the intracellular compartment. The intracellular potassium concentration is about 115 mEq. per liter, while that in the extracellular fluid is only 5 mEq. per liter. Despite this marked difference in concentration, the intra- and extracellular potassium seem to be in some sort of equilibrium, as evidenced by the fact that during potassium deprivation potassium leaves the cells and passes into the extracellular fluid, whereas during potassium administration it enters the cells from the extracellular compartment.[6]

The only exogenous source of potassium is in the diet. The average man ingests about 3-4 grams of potassium per day. Since the body does not store potassium, in a man who is in normal balance, almost all that is ingested is excreted in

*Read in Section on Gastroenterology, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

*From the Departments of Medicine, Washington University School of Medicine and the Unit I (Washington University) Medical Service of the St. Louis City Hospital.

*The determinations reported in this paper were made with the Weichselbaum-Varney flame photometer.[5]

the urine and small amounts appear in the stool and sweat.

In patients who are vomiting, potassium balance may be greatly disturbed for several reasons. First, the only source of supply, namely, that in the diet is either curtailed or eliminated altogether. Secondly, considerable quantities of potassium are lost in the vomitus. Gastric secretions contain potassium in a concentration of about 2-8 times that of the serum.[4 7] Thirdly, despite the decreased intake, the loss in the vomitus and the absence of adequate reserves of potassium in the body, the kidneys will continue to excrete significant amounts in the urine.[8] Unlike sodium, potassium is not retained or conserved by the kidneys even in the presence of a marked potassium deficiency with low serum concentrations. It is, therefore, exceedingly important for the clinician to recognize potassium deficiency and promptly institute the necessary corrective measures.

The presence of potassium deficiency in a patient is suggested by the appearance of the following clinical signs:[9] (1) muscular hypotonia and weakness, which may progress to actual paralysis, and if muscles of respiration become involved, may cause death; (2) abdominal distention, nausea, and vomiting resulting from ileus of the gastrointestinal tract; (3) sudden unexplained fall in blood pressure and (4) characteristic electrocardiographic changes due to disturbance of myocardial function.

These signs, while they are very important, especially in patients in whom there is good reason to expect potassium deficiency, are not pathognomonic. Important deficiency may be present without any recognizable clinical signs. The electrocardiogram affords a reliable method of diagnosis. It should always be used, even in conjunction with serum level determinations, since the latter measures only extracellular concentration and may be normal when a total body potassium deficit exists. The changes in the electrocardiogram associated with potassium deficiency may be summarized as follows:[9 10]

(1) The T wave is broad, low, or inverted.

(2) The Q-T interval is prolonged. This finding is to be differentiated from the similar change seen in hypocalcemia where the prolongation is due to an increase in the S-T segment and the T wave is normal. In potassium deficiency the Q-T prolongation is due to the increased duration of the T wave.[11]

(3) The S-T segment is depressed or sagging.

(4) U waves may appear.[11]

To illustrate some of the clinical manifestations and problems of potassium deficiency, the following case report is presented:

A 65-year-old white man was admitted to the St. Louis City Hospital on February 8, 1950 complaining of weakness and severe vomiting of six weeks duration. The vomiting began after an episode of excessive alcoholic intake. The patient remained confined to bed for four weeks prior to admission, and his diet consisted solely of small amounts of fluids during this period. He was brought to the hospital by his family because of the onset of mental confusion and hallucinations.

Physical Examination.—Examination revealed a well developed, malnourished, uncooperative, disoriented white man lying restlessly in bed. The temperature was 37.8° C., pulse 96 and respirations 18 per minute. The skin was dry with numerous ecchymoses on the arms. Coarse inspiratory and expiratory rhonchi were heard over the right lung base, posteriorly. The heart was normal to percussion and auscultation. The blood pressure was 110/60. The liver extended 10 cm. below the right costal margin in the midclavicular line. There was generalized muscular weakness. The knee jerks were hypoactive and the ankle jerks were absent. The Trousseau and Chvostek signs were negative.

Laboratory Data.—Urinalysis showed specific gravity 1.017, pH 6.0, sugar negative, albumin 1 plus. Microscopically one granular cast was seen, a few white and red cells per high power field, acetone was 2 plus, bilirubin negative, and urobilinogen negative. White blood cell count was 8,203. Differential disclosed 1 basophil, 21 stabs, 68 segmented forms, 9 lymphocytes, 1 monocyte. Red blood cell count was 3,570,000. Hemoglobin was 12 grams. Blood Kahn was positive (3 Kahn units). Carbon dioxide combining power of the blood was 34 mEq./1., chlorides were 67 mEq./1., calcium 3.7 mEq./1., blood urea nitrogen 5 mg. per cent, total proteins 6.0 grams per cent (albumin 3.5 grams per cent, globulin 2.5 grams per cent), cephalin cholesterol flocculation 3 plus in 48 hours, total cholesterol 118 mg. per cent, cholesterol esters 59 mg. per cent. Stool was brown, and guaiac negative. Chest roentgenogram disclosed no evidence of parenchymatous disease. Complete upper and lower gastrointestinal series revealed no abnormalities (*Fig. 1*).

The clinical diagnoses of Laennec's cirrhosis and probable alcoholic gastritis were made. The patient did very poorly, becoming so weak that he was unable to move his extremities. He continued to vomit, and remained disoriented and obtunded. He was given vigorous fluid and electrolyte therapy, including 5 per cent NaCl and 2 per cent NH_4Cl, but the alkalosis persisted.

On the 16th hospital day, the serum potassium level was found to be 2.2 mEq./1. The electrocardiogram showed prolongation of the Q-T interval and flat T waves. The patient was begun on parenteral potassium chloride. Within 24 hours there was dramatic improvement with rapid return of muscular strength and complete mental clearing. The blood electrolytes also quickly returned to within normal limits. The patient began to take food by mouth and was maintained on oral potas-

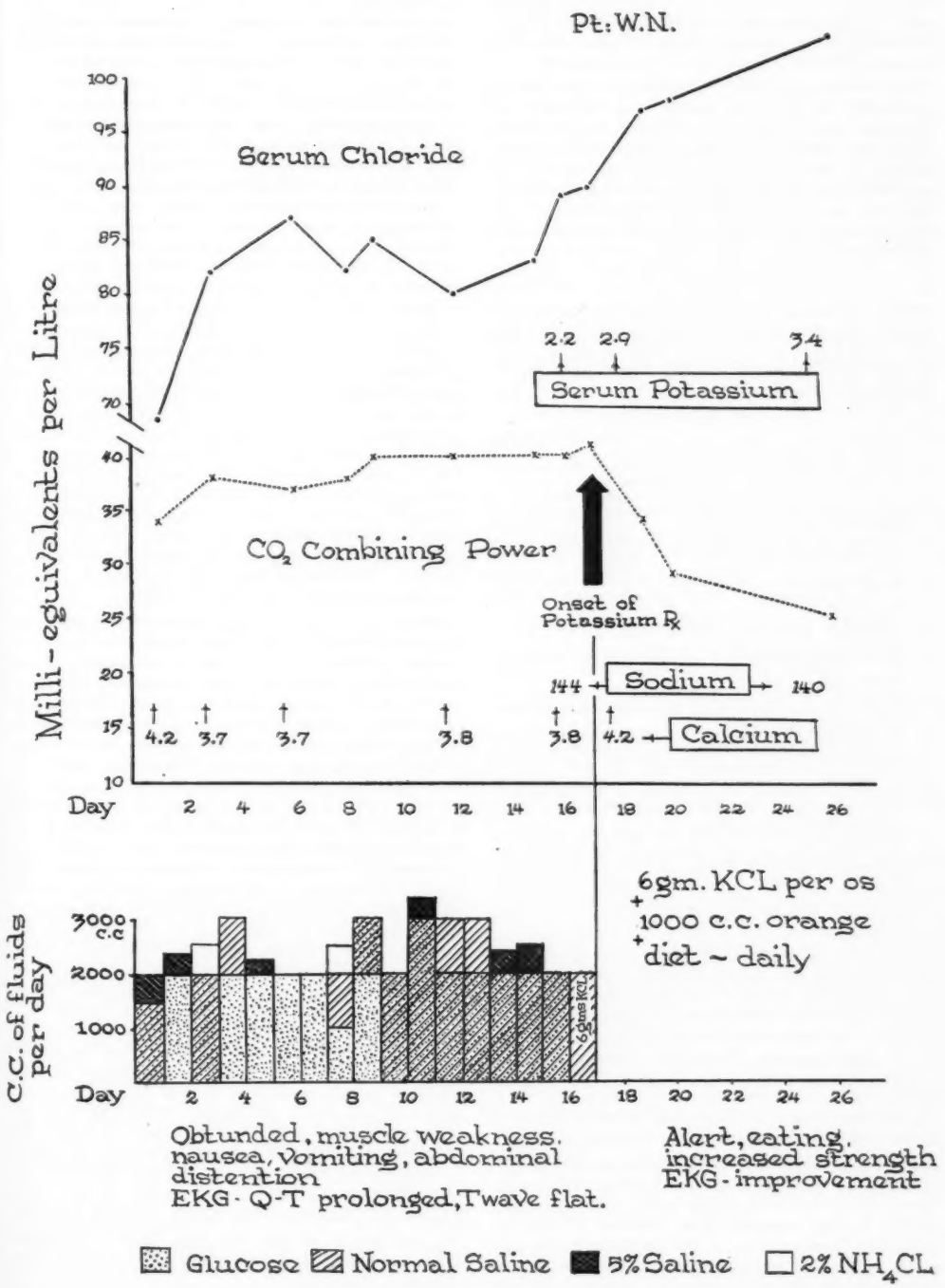

Pt: W.N.
Serum Chloride
Milli-equivalents per Litre
100
95
90
85
80
75
70
40
35
30
25
20
15
10
2.2
2.9
3.4
Serum Potassium
CO_2 Combining Power
Onset of Potassium Rx
144
Sodium
140
4.2
3.7
3.7
3.8
3.8
4.2
Calcium
Day
2 4 6 8 10 12 14 16 18 20 22 24 26
6gm. KCL per os
+ 1000 c.c. orange
+ diet ~ daily
C.C. of fluids per day
3000 c.c
2000
1000
6gms KCL
Day
2 4 6 8 10 12 14 16 18 20 22 24 26
Obtunded, muscle weakness, nausea, vomiting, abdominal distention
EKG - Q-T prolonged, T wave flat.
Alert, eating, increased strength
EKG - improvement
Glucose
Normal Saline
5% Saline
2% NH_4CL

FIG. 1

sium chloride and orange juice in addition to a soft diet. Within a few days he began sitting in a chair, and eating a regular diet. His future course was uneventful.

It was interesting to note that on the day following institution of potassium therapy, the Chvostek and Trousseau signs became positive for a short period of time. This illustrates the depressing effect of hypopotassemia or neuromuscular irritability and how it may mask the signs of latent tetany associated with alkalosis. Also the resistance of alkalosis when associated with hypopotassemia to the usual therapeutic measures is well demonstrated.

SUMMARY

The importance of potassium deficiency resulting from vomiting and inadequate food intake is emphasized and the clinical manifestations are described.

REFERENCES

1. Hartwell, J. A.; and Houguet, J. P.: Experimental Intestinal Obstruction in Dogs. J.A.M.A., **59**:82 (July 13) 1912.
2. Scudder, J.; Zwemer, R. L.; and Truszkowski, R.: Potassium in Acute Intestinal Obstruction. Surgery, **1**:74 (Jan.) 1937.
3. Cutler, E. C.; and Pijoan, M.: Certain Chemical Factors in Experimental High Intestinal Obstruction. Surg., Gyn. & Obst., **64**:892 (May) 1937.
4. Falconer, M. A.; Osterberg, A. E.; and Borgen, J. A.: Intestinal Obstruction in Man. Arch. Surg., **38**:869 (May) 1939.
5. Weichselbaum, T. E.; and Varney, P. L.: A New Method of Flame Photometry. Proc. Soc. Exper. Biol. & Med., **71**:570, 1949.
6. Hoffman, W. S.: Clinical Physiology of Potassium. J.A.M.A., **144**:1157 (Dec. 2) 1950.
7. Randall, H. T.; Habif, D. V.; Lockwood, J. S.; and Werner, S. C.: Potassium Deficiency in Surgical Patients. Surgery, **26**:341 (Sept.) 1949.
8. Tarail, R.; and Elkinton, J. R.: Potassium Deficiency and the Role of the Kidney in Its Production. J. Clin. Investigation, **28**:99 (Jan.) 1949.
9. Darrow, D. C.; and Pratt, E. L.: Fluid Therapy: Relation to Tissue Composition and the Expenditure of Water and Electrolyte. J.A.M.A., **143**:365 (May 27); **143**:432 (June 3) 1950.
10. Tarail, R.: Relation of Abnormalities in Concentration of Serum Potassium to Electrocardiographic Disturbances. Amer. J. Med., **5**:828 (Dec.) 1948.
11. Ernstene, A. C.; and Proudfit, W. L.: Differentiation of the Changes in the Q-T Interval in Hypocalcemia and Hypopotassemia. Trans. Am. Clin. & Climatol. Assn., **59**:29, 1947.

DISCUSSION (*Abstract*)

Dr. George T. Harrell, Winston-Salem, N. C.—The introduction of the flame photometer, as the authors have pointed out, makes it possible to measure quickly and accurately the concentration of potassium in serum or urine. The instrument is often quite temperamental, though, and one must know the quirks of his own machine. Measurements of the serum level of potassium give an estimate of the level of the ion in the extracellular fluid spaces, but do not indicate the intracellular content which is important in the function of cells.

The serum-extracellular equilibrium is reached rapidly. The extra-intracellular equilibrium is attained much more slowly. When one is measuring serum levels, it is quite possible to find a normal serum level but to have the intracellular content low. A low cellular concentration, as the authors have pointed out, can be indirectly detected from the alteration in function of myocardial cells as shown by serial electrocardiograms.

The introduction of the radioactive isotopic technic, by which the dilution and excretion of K^{42} are measured, permits the study of phases of potassium metabolism impossible to approach by standard chemical methods. Equilibrium between serum and cells is reached in 15 to 24 hours after the injection of the isotope. By this technic it is possible to estimate the total body content of potassium which seems to be particularly important when it is related to the weight of the individual. We have found that in normal young women the potassium content in term of milliequivalents per kilogram of weight is two-thirds that of normal young men. We have attributed the lower content to the relatively smaller proportion of muscle mass and greater proportion of fat in women as compared with men. Only by the isotopic technic is it possible to study the dynamics of potassium exchange. In experiments conducted in our laboratory and clinic by Dr. Jerry K. Aikawa, changes in rate of exchange of radiopotassium have been detected before alterations in the absolute values have been observed by flame photometry. Animals completely starved excrete in the urine an amount of potassium which can be accounted for by the breakdown of tissue; this experiment sheds light on one factor involved in potassium loss in chronic vomiting. The ratio of potassium to nitrogen indicates the relationship of this ion to protein metabolism and the ratio of potassium to phosphorus indicates its relationship to utilization of glucose. Both of these processes take place intracellularly and will be upset by the increased breakdown of tissue as well as the decreased retention of food in vomiting.

Studies on potassium in gastrointestinal disease are important because of the extent of the loss of the ion and the problems concerned with its replacement. As the authors have pointed out, large amounts of potassium may be lost by vomiting since the gastric secretions may contain 4 to 10 times the content of potassium found in serum. It should be recalled that constant gastric suction as used in preparation of patients for operation will result in the same loss of ions as would vomiting. A loss similar to that of vomiting may follow diarrhea since the potassium content of intestinal fluids is roughly twice that of the serum. Potassium may be lost from the body when patients with cirrhosis of the liver are treated by repeated paracenteses or with diuretics. Interesting studies on the potassium deficit in cirrhosis have been done in our clinic by Dr. Malcolm Tyor in the course of the experiments on albumin reported before this section yesterday. Vomiting which progresses to the point of bleeding and shock may result in the so-called lower nephron syndrome. When renal function is thus depressed potassium is retained by the body and signs of toxicity may result. If shock persists for any length of time, the tissue anoxia produces an alteration in permeability of cell membranes so that potassium is lost from cells into serum, temporarily giving high levels in the serum in the presence of a cellular deficit. The potassium loss in diabetic acidosis, apparently as a result of attempts by the kidney to neutralize the increased amounts of organic acids, is well known. In our clinic experiments have shown that poorly regulated diabetics who are not in acidosis may also show a potassium deficit, apparently from the interference with intracellular utilization of glucose.

The role of stress from any type of disease and the resulting increase in secretion of ACTH and adrenal cortical hormones is not yet clear. The administration of

these hormones therapeutically is known to increase the excretion of potassium and to induce a deficit which we have found on occasion to be of considerable magnitude. We should recall that potassium and sodium metabolism are closely related. The development of the low salt syndrome from restriction of dietary intake of sodium or from its loss through repeated administration of mercurial diuretics may also upset the potassium balance. The increasing use of ion exchange resins in the treatment of gastrointestinal disturbances, such as peptic ulcer and cirrhosis, is another method by which potassium content may be altered. One should know precisely the characteristics of the resin which he is using to be sure that potassium is not lost in the gastrointestinal secretions exactly as it would be in vomiting or diarrhea.

When a potassium deficit has been detected, it should be corrected by oral administration of the ion if possible. Of course, in the presence of vomiting this method of replacement is not feasible. One should recall that the amount of potassium ordinarily taken daily in the diet of the average person is equivalent to the total amount found in the extracellular fluid spaces of the body. It is thus obvious why a deficiency detectable by a lowered serum concentration may develop rapidly. Since potassium is found chiefly within cells, as the authors have pointed out, an animal source of muscle cells, meat or meat extracts, offers a readily available source with a high content. If the patient cannot retain meat, potassium can be administered intramuscularly or intravenously since commercially the chloride salt is available already prepared in ampules. The familiar Ringer's solution which is available in most hospitals contains a small amount of potassium. When the ion is given parenterally, it should be given at a very slow rate, since its accumulation in the blood and extracellular fluid spaces will produce toxic effects before equilibrium is reached with the intracellular space. Whenever it is possible, one should anticipate the development of potassium deficiencies and prevent them. If renal function is adequate, the additional administration of potassium chloride in the presence of vomiting, diarrhea, acidosis, or other gastrointestinal disease may improve the results to be expected from present types of therapy.

Dr. E. E. Muirhead, Dallas, Tex.—In recent years studies, such as those presented by Drs. Shatz and Catanzaro, have served to emphasize various abnormalities in the distribution of potassium in the body. Increments in the extracellular potassium, which are especially dangerous because of their cardiotoxic effects, are usually the result either of the rapid intravenous administration of this ion or due to failure of the kidneys to excrete this ion in renal disease. However, it is remarkable how many patients with serious but recoverable acute renal failure fail to exhibit hyperkalemia when the potassium intake is restricted. Decrements of potassium, on the other hand, result from the excessive loss through various fluids escaping from the body. Drs. Shatz and Catanzaro have emphasized the loss through one such portal, namely, via the upper gastrointestinal secretions as a result of vomiting. Similar disturbances may result from the institution of suction or through various fistulae. Diarrhea is the second prominent source of potassium loss as discussed by Dr. Harrell. Ordinarily losses through sweating are considered negligible, although under special conditions, as in induced fever therapy, this source may assume a more prominent position. The other major source of potassium loss is the urine. Tarail and Elkington have emphasized the constant loss in the urine, even in the presence of normal kidneys, when the intake is curtailed, as in gastrointestinal disorders. Under these circumstances a constant loss of 50 mEq. (about 2 grams) of potassium per day may accrue, in time, into a substantial deficit. The presence of abnormal kidneys may of itself lead to a prominent potassium deficit. Rarely in chronic Bright's disease and not so rarely during the early recovery (diuretic) phase of lower nephron nephrosis this complication develops. In the latter condition daily losses may vary between 50 and over 200 mEq. (2 to over 8 grams) per day. Consequently, it is advisable to administer potassium salts, as potassium chloride, empirically during the diuresis following acute renal failure. There is no rule that will cover all cases but 4 to 6 grams of potassium chloride (50 to 80 mEq. K) for every three liters of urine will decrease the possibility of a serious deficit. On occasions greater quantities are necessary to prevent deficits.

ATTENUATED VIRUS IN AUTOGENOUS BLOOD SERUM AS A THERAPEUTIC AGENT IN HERPES ZOSTER*

By CHARLES P. BONDURANT, M.D.†
Oklahoma City, Oklahoma

It is proposed in this discussion to make a report concerning the use of attenuated or inactivated viruses in autogenous blood serum as a therapeutic measure in herpes zoster. The preliminary report of this work was given on the program of the Society for Investigative Dermatology in 1950. This principle of therapy applies to diseases of viral etiology in general, but this discussion will be confined to that part of the problem which concerns herpes zoster. There are many proposed methods of management of this disease but few methods are seen that treat the disease as an infection, using as a basis of therapy the production of a better immunity or a stimulation of the immune processes. It is a well known fact that herpes zoster is a self-limited disease, that it produces its own lasting immunity, this immunity usually protecting the patient for life. This one episode characteristic of this disease suggests strongly its infectious origin or etiology.

---

*Read in Section on Dermatology and Syphilology, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

†Professor of Dermatology and Syphilology, University of Oklahoma School of Medicine, Oklahoma City, Oklahoma.

Herpes zoster is a severely painful and incapacitating disease found usually in adults, and is characterized by an inflammatory process which involves the dorsal root ganglia, or extramedullary ganglia of the cranial or spinal nerves. This inflammatory process is accompanied by crops of vesicles identical with those of varicella, and limited to the area supplied by these sensory nerves. Although herpes zoster was described in Greek literature it was von Bärensprung[1 2] in 1862 who first recorded observations connecting the area of skin involved by this eruption to its corresponding dorsal root ganglion. Landouzy in 1884 and Levaditi[3] in 1926, on clinical grounds only, suggested its infectious etiology. Head and Campbell[4] working together in 1900 called attention to the one episode characteristic of this disease and classically described the neuropathology. Lipschütz[5] in 1921 described the histopathological changes in the vesicles. In 1909 von Bokay[6] suggested its relationship to varicella and presented numerous cases to verify his observations. The infectious nature of herpes zoster was put on a more sound basis when Kundratitz[7] in 1925 was able to inoculate 22 children with the vesicular fluid and transmit the disease to 14 of these. It has been difficult to establish the incubation period of herpes zoster but 7 to 14 days has been fairly well accepted, a somewhat shorter period than that of varicella. Other factors have been thought to contribute to the incidence of this infection; insults to the susceptible dorsal nerve roots, such as those caused by arsenic, tumors, leukemia and tuberculosis. I have seen many cases which I thought could be attributed to anxiety, nervousness, exhaustion, war, and so on. At the onset of this condition these patients are found to have some fever, malaise, pain, and often considerable tenderness along the involved dorsal roots and their corresponding skin areas. The vesicles appear about the third to fourth day completing the clinical picture upon which the diagnosis is made. By this time, however, the ganglia are well involved and pain and tenderness are at their height. It is an old process at this stage. In the cases where this involvement of the ganglia is extensive the motor roots may be involved resulting in paralysis. This paralysis is usually temporary but may be permanent in severe cases where scar tissue replaces the nerve structure. Zoster ophthalmicus and involvement of the gasserian ganglion has been found to be very serious, resulting in iridocyclitis, scleritis and keratitis. Anesthesia of the cornea is common and corneal ulcer complicates this disease too frequently. It has been estimated that in approximately 50 per cent of cephalic cases of herpes zoster some type of paralysis occurs. There is many times a lymphocytosis in the spinal fluid. A persistent neuralgia following convalescence in older subjects is the most common and troublesome sequel.

The virus etiology of herpes zoster and its close resemblance to varicella has been a subject of considerable comment for some time. It is difficult to discuss one disease without the other being considered. Since von Bokay's original observations many data have been accumulated on the similarity of the two diseases. Both viruses are apparently very similar in size, the diameters of each having been estimated at from 150 to 250 millimicra. The viruses are most numerous in the vesicle fluid one to two days after the appearance of the lesions. The convalescent sera of herpes zoster has been found effectively to agglutinate that of convalescent varicella patients, thus definitely exhibiting antigenic characteristics and helping to explain the lasting and strong immunity which the one episode characteristic of herpes zoster affords. The number of such recorded incidents is too great to explain the question on a chance basis (the School Epidemics Committee, 1938). The histopathology of the more serious cases is characterized by an infiltration of small round cells and red blood cells in and around the posterior roots. This is followed by necrosis of nerve cells and fibers and an inflammatory reaction in the ganglion sheath. The corresponding fibers of the spinal cord may undergo degeneration. In the milder cases little or no damage is done.

The virus etiology of herpes zoster is well established and a study of some of the characteristics of virus infection in general, and this virus in particular, is interesting. A great amount of study is being done, and the biological nature and composition of the viruses are gradually unfolding. In these studies the names of Stanley, Rivers, Wyckoff, Green, Knight, Tang, and a host of others are prominent. When we review the evidence to date the conclusion that the viruses are minute, strongly parasitic microorganisms with highly individual characteristics, is inescapable. These organisms exhibit many of the traits common to the bacteria family, pro-

ducing definite and distinct clinical pictures (smallpox, chickenpox, herpes zoster, rabies, mumps, poliomyelitis, and so on). The outstanding clinical characteristic of the viruses is their known ability to produce a strong and lasting immunity, a group of one-episode diseases. The biological mechanism of this immunity, as in all immunity, is little understood. From the observations of Andrewes[8] (1930) and others, there is little doubt that specific antibodies play an important role in the immunity to these virus infections.

Attenuation, or inactivation, is one of the oldest forms of combatting infectious disease, and strangely enough the most successful and earliest work was done on diseases of viral etiology. Jenner, in 1798, knew nothing of virus infection but he used the attenuated virus of cowpox to produce his vaccination for smallpox. In 1884, Pasteur could not find an organism in rabies and he knew the etiological factor passed his finest filter. For want of a name he called this material a "virus" which is the Latin word for poison. He then modified the pathogenicity of the virus for its natural host and by attenuation or inactivation developed his famous prophylaxis for rabies.

In reviewing these long tested methods, where attenuation or a partial killing of the organism is the fundamental factor in the production of this artificial immunity, it is easy to assume that this protecting force is not all produced at once and that it is not all the result of completely killed organisms. This same process is observed in the spontaneous cure of bacterial disease. This immunity is a product of the forces of natural immune processes, these being aided by the presence in the host of organisms in all the stages of the dying process. It follows that the use of inactivated, attenuated, or partially killed viruses in autogenous tissue or blood could be a logical and effective procedure in the production of immunity. In this procedure where autogenous blood serum is used the biological identity of a particular virus with its morphological characteristics is unnecessary. The autogenous factor removes the many problems ordinarily encountered in transfusion therapy. It has been repeatedly shown, as stated above, that the blood stream carries some of the antigenic factors and the inclusion bodies have been demonstrated in blood cells. The blood serum taken in the active phase of the disease can be assumed to contain organisms. The blood for this process is drawn

Case No.	Age	Sex	Treatment Started	Degree of Involvement	Post-Herpetic Neuritis	Location	No. Daily Doses	Results	Spinal Fluid Finding
1	24	M	1 day	Moderate	None	Posterior right cervical	6	Healed 6 days	None
2	86	M	5 days	Severe	Prolonged	Left facial	10	Healed 16 days	Lymphocytosis
3	65	F	2 days	Mild	None	12th dorsal right	5	Symptom free on 8th day	None
4	87	F	2 weeks	Severe	Marked right hip and leg	Right hip and thigh	12	Slow healing	None
5	51	F	3 days	Moderately severe	Mild facial paralysis	Right facial	9	Skin lesions 11 days Paralysis 5 weeks	Lymphocytosis
6	83	M	4 days	Severe	Mild	Left ophthalmicus	8	Symptom free 2 weeks	None
7	37	M	1 day	Moderately severe	None	5th and 6th right dorsal	11	Symptom free 12 days	None
8	71	F	3 days	Moderately severe	Prolonged	Left shoulder and neck	10	Course prolonged	None
9	43	F	2 days	Moderately severe	None	Right facial	9	Clear 11th day	None
10	67	F	3 days	Severe	None	Right ophthalmicus	10	Symptom free 12th day	None

TABLE 1

and prepared under aseptic conditions, as follows: 30 cc. of blood is drawn, allowed to coagulate in ice box, clots separated, centrifuged, and serum drawn off. This serum is then heated in a hot water bath at 56° C. for 30 minutes. It is then cooled and injected intramuscularly. It is important to keep the water bath below the coagulation temperature which is 60° C. The attenuated serum is given in daily doses of 5 cc. each, usually in a course of 6 to 10 doses. There have been no immediate reactions noted but three of the cases have developed urticarial lesions during the second week. These subsided on the usual management of urticaria. (I am now using whole blood prepared with anticoagulants in the same manner as for transfusion: inactivating it for 20 minutes by the same method. I feel, to date, that the serum is the better of the two). The treatment is far less effective in the mild cases. It seems that the case must be of enough magnitude to develop a fairly sharp and virulent reaction.

The diagnosis of herpes zoster cannot be effectively made until the vesicular stage of the disease develops, and I feel that the blood carries its maximum virus content about this time. The main purpose of the treatment is to produce as much immunity protection as possible at the earliest stage, and prevent as much as possible the development of the destructive processes referred to earlier in this discussion. The importance then of early diagnosis is paramount and cannot be stressed too much. The incidence of post-herpetic pain is found to increase in proportion to the delay in the starting of treatment. Other measures used are the usual local applications and medication for the control of pain. I have found that the usual course of the disease is shortened in younger individuals to only a few days. In the older patients and more severe cases the skin lesions are of prolonged duration. Herpes zoster in the aged is a major problem and many terminate fatally.

It is difficult to estimate what is normally the course of a case of herpes zoster. This is a variable factor and the degree of severity tends to determine this point. A table of ten cases is given to show some of the points under discussion in this consideration.

CONCLUSIONS

This type of therapy may be an aid in the management of herpes zoster.

BIBLIOGRAPHY

1. von Barensprung, F. G. E.: Fernere Beitrage zur Kenntniss des Zoster. Ann. Charite-Krankenhauses, **10**:1 Hft., 37-54, 1862.
2. von Barensprung, F. G. F.: Neue Beobachtungen uber Herpes. Ann. Charite-Krankenhauses, **10**:1 Hft., 123-143, 1862.
3. Levaditi, C.: L'Herpes et le zona. Paris: Masson, 1926.
4. Head, H.; and Campbell, A. W.: The Pathology of Herpes Zoster and Its Bearing on Sensory Localization. Brain, **23**: 353-523, 1900.
5. Lipschutz, B.: Untersuchungen uber die Atiologie der Krankheiten der Herpesgruppe (Herpes Zoster, Herpes Genitalis, Herpes Febrilis). Arch. Dermatol. u. Syph., Orig., **136**:428-482, 1921.
6. von Bokay, J.: Ueber den atiologischen Zusamenenhang der Varizellen mit gewissen Fallen von Herpes Zoster. Wien. klin. Wchnschr., **22**:1323-1326, 1909.
7. Kundratitz, K.: Experimentelle Ubertragungen von Herpes Zoster auf Menschen und due Beziehungen von Herpes Zoster zu Varicellen. Ztschr. f. Kinderhelik, **39**:379-387, 1925.
8. Andrewes, C. H.: Tissue Culture in the Study of Immunity to Herpes. J. Path. and Bact., **33**:301-312, 1930.

DISCUSSION (*Abstract*)

Dr. Thomas W. Murrell, Richmond, Va.—Dr. Bondurant is employing an old remedy, autohemotherapy, in a specific way guided by a specific theory. What autohemotherapy does and how results are accomplished has always been mysterious, supposedly affecting immune processes. One of the older clinicians many years ago in discussing the effect of autohemotherapy on recalcitrant psoriasis said, "I only know I put something back I did not take out." It is hard to conceive of a situation more difficult to evaluate.

The late Dr. J. N. Rounselle firmly believed in the efficacy of neoarsphenamine in the therapy of herpes zoster. We tried this and at times the results were dramatic, but in other cases there was no change, so one never knew what was due to therapy and what was due to the nature of the case, and the treatment was abandoned.

Theoretically, serum from another patient recovered from the attack should be of value. We have used this only once with no apparent help.

If from the series of cases presented, Dr. Bondurant feels there is enough improvement to justify continuing this work, a larger series may definitely prove his conviction. Without this it must remain an open question.

Dr. Howard Hailey, Atlanta, Ga.—I have reviewed the cases of herpes zoster which I have seen since 1934. The disease has occurred in 125 males and 126 females. The youngest patient was an eight-year-old boy. The oldest patient was a woman aged 83. In this series there was a case of paralysis in a boy about ten years of age. I attributed the paralysis to edema pressure at the foramen of exit of the facial nerve. The paralysis looked like the usual Bell's palsy. Recovery was prompt and complete. There was not a single case of involvement of the cornea in this series of patients with herpes zoster. I believe that eye involvement in herpes zoster is rare and the complication of eye involvement has been overemphasized in most textbooks. Dr. Bondurant will no doubt continue in this investigative work and I trust that he will report confirmed findings at a later date. In closing, I wish the essayist would inform us as to the number of patients with corneal involvement whom he has observed, and whether there was an appreciable amount of subsequent damage to vision.

Dr. Onis G. Hazel, Oklahoma City, Okla.—We recognize the immunizing effect of cowpox vaccine in preventing smallpox, the use of immune globulin to attenuate or prevent measles, and viral suspensions or filtrates to prevent yellow fever or attenuate virus A and B types of influenza. We are not well informed about using inactivated viruses in treating virus diseases once the disease has developed. It is quite possible that the author has given us an example in which an autogenous inactivated virus can reduce the severity of cases of herpes zoster. It may reduce hemorrhage and lymphocytic infiltration of the involved nerves. I know that Dr. Bondurant, too, is conscious of the difficulty in evaluating therapy in any self-limited disease which may vary greatly in degree of severity.

Dr. C. Ferd Lehmann, San Antonio, Tex.—None of the recommended treatments for herpes zoster is effective in 100 per cent of the cases, or is specific. I use iodides, calcium gluconate, sometimes autohemotherapy, salicylates, and x-ray treatments to the paravertebral ganglia. No antibiotic is effective, except in controlling a superimposed infection. The post-herpetic pain is unpredictable. Some with severe herpetic eruption have very little pain and others with very mild objective symptoms complain bitterly for months.

I should like to ask Dr. Bondurant whether he has used the prepared serum on others than the donor, and whether he has done any work towards establishing what we might call a "herpes serum bank."

Dr. Thomas B. Hall, Kansas City, Mo.—Over the years, I have been considerably impressed by the role of stress in precipitating herpes zoster.

Several years ago, at the Kansas City General Hospital, we had a skinny boy about ten years old, who was playing leap-frog. A big fat boy jumped on him, straddling him out, and he developed a terrific bilateral herpes zoster of both lower extremities. I have seen several similar instances, less dramatic.

Dr. D. Truett Gandy, Houston, Tex.—I should like to comment on the persistent post-zoster pain which we sometimes encounter, especially in elderly patients. We have all had this experience. It can be a critical problem. I know of no formula for combatting it successfully, aside from the conventional sedative drugs used to control pain.

Dr. Bondurant (closing).—A series of cases so short as this one offers no conclusive facts, but it does serve to call attention to some fundamental things in the production of immunity in viral disease. I wish to emphasize the importance of the time factor in early diagnosis and treatment.

In answer to Dr. Hailey's question I have seen two cases in which I thought there was involvement of the cornea. The common complications in the cornea are secondary in nature and come as a result of corneal anesthesia which is fairly common in ophthalmic cases. This is due to involvement of nerve tissue. The way to demonstrate this is to draw a twisted thread of cotton over the non-affected cornea; then to do the same on the opposite side. In this respect, I have seen no permanent damage to vision.

Dr. Hazel has seen several of these cases and I have discussed with him at length many of the principles involved in this type of therapy. We have agreed that the type of treatment which has been described, due to the self-limited pathological processes involved, promises only to reduce the severity of the disease. I am glad he has spoken of applying this principle in the approach to other diseases for which we have no satisfactory therapy. This is being done.

In answer to Dr. Lehmann's question concerning the use of a prepared serum other than autogenous serum, and of a herpes serum bank, I should like to say that it is a good thought but I have not done any work on it. I have thought of fortifying the autogenous serum before attenuation with some fluid from the herpes vesicles, but I have not done this, either.

Nervous exhaustion and stress play a part in the incidence of herpes zoster. It may be comparable to the physical condition of a patient before he takes a bad cold.

Post-herpetic pain may be troublesome. This calls attention again to the importance of starting therapy at the earliest possible time.

The body, on the whole, does a good job of caring for itself. It cures most of its own ills, and I believe that we cannot find a more logical agent to utilize than immunization based on logical biological principles. The use of attenuated organisms is only a lift in attaining quicker and stronger immunity.

CARCINOMA OF OVARY: NEWER ASPECTS*

By Wm. F. Guerriero, M.D., F.A.C.S.
J. W. Tabler, M.D.
and
Charles Bruce, M.D.
Dallas, Texas

Carcinoma of the ovary is an entity which demands more attention. Marchetti,[1] in an extensive survey, found 15 per cent of all female genital cancer to be ovarian in origin. Speert[2] says that cancer of the ovary ranks fourth among neoplasms as a cause of death in women over the age of forty. In the year 1945, in white women over the age of forty, the mortality was 17.2 per 100,000 of the United States population.

*Read in Section on Gynecology, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

*From the Department of Obstetrics and Gynecology, Baylor University Hospital, Dallas, Texas.

During that year, 4,386 women expired as a result of carcinoma of the ovary.[2] This figure also approximates the maternal mortality rate for that year.

We are conscious of the fact that physicians exhibit an attitude of futility in regard to ovarian carcinoma. Certainly, the obstetricians had no such attitude about the problems of maternal mortality. Thus, a lowering of the mortality of ovarian carcinoma can be accomplished by a more vigorous interest in prevention and early diagnosis and a more extensive surgical approach to therapy.

That carcinoma of the ovary is an all-inclusive term depicting many and varied forms of ovarian tumors is not always fully appreciated and considered by the clinician. *Table 1* is a working classification of all the various types of ovarian malignancy. *Table 2* shows the types of ovarian carcinoma from a collected series of 553 ovarian tumors in a period from June 1, 1946 to June 1, 1951, at Baylor University Hospital of Dallas, Texas. During this same period there were reported by the pathologist three granulosa cell, one thecoma, and one arrhenoblastoma as benign tumors. We are making an attempt to survey these patients since Henderson's[7] report that the recurrence rate of carcinoma in granulosa cell tumors and arrhenoblastoma warranted more extensive surgery in these cases.

The problem of whether some of these tumors arise from precancerous ovarian lesions is also to be considered. Yet little thought has been given this. It is evident that from a biologic standpoint, all types of new growths of the ovary are closely related to malignancy. At times, these may be the source of cancer, either by appearance of malignant areas within them or through a change in their structure toward the malignant form.[3]

The incidence of carcinoma of the ovary is difficult to assess. Certainly varied confusing reports are found in the literature. Probably the most accurate is Meyer's collective statistics in which he noted 14.9 per cent of all ovarian tumors to be malignant. In our series it was found that of 553 ovarian neoplasms, 75 or 13.6 per cent were malignant.

The young patient with an ovarian tumor over 5 cm. in size has been neglected as a suspect of cancer too often on the assumption that such women under 40 years of age have a very low incidence of ovarian cancer. Our series fails to confirm this thought. Under age 30, we note an incidence of malignancy of 6 per cent as seen in *Graph 1* and *Table 3*. Of further interest is the 6.7 per cent incidence under age 40, the 21 per cent above age 40, and the 27.7 per cent above age 50.

This being true, the only treatment for any ovarian tumor which is over 5 cm. in size, and which persists in the young for over 60 days,

CLASSIFICATION OVARIAN MALIGNANCY

(I) Proliferative Tumors
- (A) Pseudomucinous cystadenocarcinoma
- (B) Papillary serous cystadenocarcinoma
- (C) Primary carcinoma (solid)
  - (a) Adenocarcinoma non or papillary
  - (b) Medullary carcinoma
  - (c) Simplex carcinoma
  - (d) Scirrhous carcinoma
  - (e) Alveolar carcinoma
  - (f) Plexiform carcinoma
- (D) Dysontogenic or special
  - (a) Granulosa cell, mild
  - (b) Arrhenoblastoma, very
  - (c) Dysgerminoma, very
  - (d) Theconea mild
  - (e) Luteoma

(II) Embryonal
- (A) Teratoma
- (B) Dermoid with epidermoid carcinoma

(III) Endothelial connective tissue
- (A) Mesonephroma sarcoma

(IV) Secondary
- (A) Simple adenocarcinoma
- (B) Krukenberg
- (C) Epidermoid
- (D) Choreoepithelioma
- (E) Hypernephroma

TABLE 1

TYPES OF OVARIAN CANCER

(Period June 1, 1946 to June 1, 1951, Baylor University Hospital, Dallas, Texas)

	Number	Per Cent
(I) Epithelial		
(A) Pseudomucinous cystadenocarcinoma	13	17.33
(B) Papillary serous cystadenocarcinoma	34	45.33
(C) Primary carcinoma adenocarcinoma	26	34.66
(II) Dysontogenic		
(A) Granular cell carcinoma	1	1.34
(III) Embryonal		
(A) Teratoma	1	1.34
Total	75	100.00

TABLE 2

is immediate laparotomy. Any pelvic mass which cannot be definitely proven to be other than ovarian should be suspected as such until proven otherwise at surgery. Frequently, supposed myoma and pyosalpinx are treated conservatively, and it is found too late that they were ovarian carcinomas.

In a consideration of symptoms, Block[4] says:

". . . Symptomless onset and symptomless progress to incurability constitute the natural history of ovarian carcinoma."

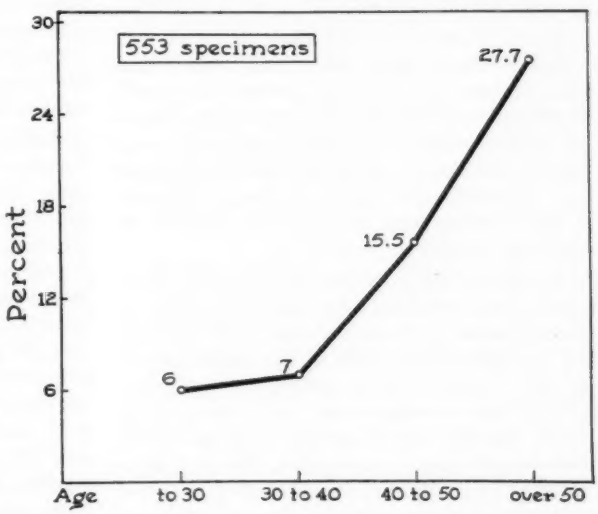
The question of malignancy can be determined definitely and with finality only by histologic study. If possible, it is essential that the pathologist be invited to be present at the surgical procedure for consultation, and to give an immediate microscopic opinion by frozen section. This should never relieve the surgeon from a responsibility of knowledge concerning every characteristic of ovarian neoplasms. One must remember, however, that frequently carcinoma is present in only a small area of one of the multilocular cysts. For a concise description, we refer the reader to the works of Novak[5] and Dockerty.[6]

Preoperative preparation of all patients undergoing surgery for ovarian or other pelvic masses should be adequate. Chest, gastrointestinal and genitourinary x-rays, bowel sterilization, restoration of adequate blood volume, an assessment by a thorough history and examination of the patient's general physical status with a proper choice of an adequate anesthetic agent, are essential preoperative requisites. Consideration must be given the fact that many ovarian carcinomas are secondary to cancer of the upper gastrointestinal tract, colon, breasts, and uterus, so that a careful evaluation of these areas should be made prior to surgery in search of a possible primary site. As a result of these preparations, age should never be a contraindication to surgery. Preoperative irradiation is not recommended, as will be discussed later.

Abdominal centesis in patients with ascites and ovarian tumors is needless meddling. The value in diagnosis is negligible since surgery is the preferred treatment, and the risk of spread of tumor cells is great.

At the time of operation when the diagnosis of cancer of the ovary becomes an actuality, the degree of surgical extirpation will depend on the

PER CENT INCIDENCE MALIGNANCY BY AGE GROUPS



GRAPH 1

INCIDENCE OF OVARIAN CARCINOMA BY AGE GROUPS

AGE	To 30		30 to 40		40 to 50		Over 50		Total	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Malignant	7	6	12	7	23	15.5	33	27.7	75	13.6
Benign	108	94	159	93	125	84.5	86	72.3	478	86.4
Total	115	100	171	100	148	100	119	100	553	100

TABLE 3

extent of the cancer process and its type. The extension and type of tumor are also the greatest factors in prognosis. The Sloane Hospital series showed that of 71 cases in which the tumor was confined to one or both ovaries, the five-year cure rate was 60 per cent. In all save the differentiated tumors, which comprise about 20 per cent of the total, the prognosis is poor.[6] Solid ovarian carcinomas are usually bilateral and carry a mortality of 80 per cent in five years. Certainly, the predominant rule should always be for a complete removal of the cancer process to include the entire pelvic viscera, and in some, the omentum, bowel and bladder. In some, the extension does not permit even removal of the primary tumor mass. When this occurs, irradiation and then repeat surgery will be successful in many instances. Parks[7] and others have reported success in the management of several patients in this manner.

Every effort should be made to remove the primary tumor mass, since many cases have been reported in which the procedure caused a prolongation of life past five years. The failure of surgical attack is certainly responsible for a large percentage of mortality. In our series, 90 per cent of the patients were closed with only a biopsy having been done, and the other 10 per cent had incomplete surgery.

We should like to offer a procedure which has surely been employed by many, but to our knowledge has not been described in the literature, for determining the status of the apparently uninvolved ovary in gross unilateral ovarian carcinoma when conservatism is desired in the young female. After careful isolation of the uninvolved ovary is completed, then a bivalve biopsy section through its entirety is removed both for immediate gross and histologic study. This should give a measure of accuracy as to the status of the grossly uninvolved ovary.

Irradiation has been extensively employed with good results in various forms of malignancy. However, in many instances it has been poorly and injudiciously elected as a therapeutic agent. Of all the malignancy treated by irradiation, ovarian carcinoma has been and still is the least understood and most abused.

Logical irradiation requires a thorough knowledge of the characteristics of ovarian carcinoma as well as a proper understanding of irradiation therapeusis itself.

The widespread extension of carcinoma of the ovary produced mainly by ascitic fluid makes the adequate use of irradiation difficult. This and the fact that ovarian carcinoma shows a varied response to irradiation therapy accounts for the indifferent results from its use. An exception to lack of sensitivity to roentgen therapy is the dysgerminoma. This tumor is very sensitive and all areas of metastasis should be irradiated. The use of preoperative irradiation in suspect cases of ovarian cancer is clarified by Randall and Hall's[8] report that of 218 women over the age of 50 with ovarian tumors who received preoperative irradiation, only 131 or 60 per cent actually had ovarian cancer. Thus, irradiation preoperatively in such cases is best withheld. Parks has reported three cases of inoperable papillary cystadenocarcinoma which, when given deep roentgen therapy, became operable. The tumors and widespread extensions regressed in size so that at repeat surgery removal was possible. Two are alive eight and twelve years later, and one died after five years of another unrelated carcinoma.

Taylor and Greely[3] have found irradiation singularly inefficient in the cure or alleviation of cases of peritoneal involvement. Walter, Bachman and Harris[14] are more optimistic as to its value. They find no increased value in cases which are primary, unilateral and completely removable, where the entire tumor mass and local metastasis are removed or with advanced carcinomatosis peritonei. However, in the group in which only local metastases are present, yet the growth is not completely removable, irradiation is of benefit statistically. In this series 50 per cent of the patients received deep roentgen therapy, evidently as a means of therapy since these were all supposedly inoperable cases in which only a biopsy was done. No result of the therapy could be evaluated from the charts reviewed.

Irradiation should be used postoperatively even though the sensitivity of ovarian carcinoma varies. Enough reports show the occasional case in which it is of benefit. It might be especially worthwhile in instances such as Parks reported. Under no circumstances should it ever be used before as extensive surgery as possible is employed.

The first aim of medicine is to prevent disease. The second is, by treatment to stop the progress or eradicate disease. Since the etiology of cancer

is unknown, our efforts have been confined to treatment. In cancer of the ovary, our efforts have been so futile that in most instances they have not succeeded even in stopping its progress to any extent.

Crossen,[15] in 1942, advocated two rules which he thought would place the physician in a position to accomplish both of the above goals in carcinoma of the ovary. These were: (1) insistence upon frequent periodic examinations of the pelvis; (2) removal of the involuting ovaries whenever the abdomen is opened for surgery in women past 45 years of age.

Everyone agrees with the first concept, though it is sadly neglected by many physicians. The second can always evoke much discussion. However, if we accept all the facts concerning ovarian cancer, towit: symptomless, insidious onset, rapid spread and the inadequacy of present curative measures with a resulting 85 to 90 per cent mortality, we may wish to accept prophylactic oophorectomy in women past 40 to 45 years of age. The loss of ovarian secretions can be adequately compensated for by oral medication.

Speert has shown that of 260 patients with ovarian cancer, 67 or 26 per cent had previous surgery of one form or another. In 45 or 52 per cent, the patient was 40 years or older at the time of her initial surgery. More striking is the fact that 25, or 29 per cent of these, were operated upon under two years prior to the discovery of carcinoma of the ovary. Montgomery's[9] figures show 21 per cent incidence of previous relevant operations in a study of ovarian carcinoma in 99 patients.

In our series of 75 cases, 36 or 47.4 per cent had a previous surgical experience. Astoundingly, 25 of these were beyond 40 years of age, and of these, 17 had been operated upon less than two years previously.

In view of the above findings, serious consideration should be given Crossen's suggestions. This is a decision which may well be as important a prophylactic therapy for carcinoma of the ovary as was the adoption of total hysterectomy in carcinoma of the cervix.

Reports vary as to the efficacy of the steroid sex hormones to produce any beneficial effects in carcinoma of the ovary.[10] Taylor[11] says the analogy between carcinoma of the breast and prostate with ovarian carcinoma is not a true one. The former are part of the reproductive system whereas the latter is a derivative of either the coelomic endothelium or of intestinal components of teratomas. Like irradiation, they may be used with the hope of some result.

Mortality studies as reviewed by Munnell and Taylor[12] vary as to five-year cure rates from 6.3 to 65.4 per cent. However, most studies report less than 15 per cent survival over five years. Wheelock, Fennell, and Meigs[13] report a five-year survival rate of 19 cases or 28.4 per cent in 77 cases. They found survival rates to correlate with the histologic type of the malignancy. This variation is probably due to the differences in extent of the disease and the types of tumor involved in the various reports. We could not secure an adequate followup in our series. However, 5 per cent died immediately, another 6 per cent within three months, and the remaining were discharged with a very poor prognosis.

CONCLUSION

A deeper interest in the entity, ovarian carcinoma, is needed.

A request that Crossen's decision advocating more frequent pelvic examinations and a prophylactic removal of the involuting ovaries be given more consideration is presented.

BIBLIOGRAPHY

1. Marchetti, Andrew A.: Consideration of Ovarian Tumors with Special Reference to Their Malignant Potentialities. S. Clin. N. Amer., **30**:1767-1775 (Dec.) 1950.
2. Speert, Harold: Prophylaxis of Ovarian Cancer. Ann. Surg., **129**:468-475 (Apr.) 1949.
3. Taylor, H. C., Jr.; and Greely, A. V.: Factors Influencing the End Results in Carcinoma of the Ovary. Surg., Gynec. & Obst., **74**:928-934, 1942.
4. Block, Frank B.: Ovarian Tumors. Amer. J. Med. Sci., **212**:738-754 (Dec.) 1946.
5. Novak, Emil: Gynecology and Obstetrics Pathology. Philadelphia: W. B. Saunders Co., 1947.
6. Dockerty, Malcolm B.: Ovarian Neoplasms. Surg., Gyn. & Obst., **81**:179-204 (Nov.) 1945.
7. Parks, T. J.: Carcinoma Ovary Treated Preoperatively by Deep Roentgen Therapy. Am. J. Obst. & Gynec., **49**:676-685, 1945.
8. Randall, Clyde L.; and Hall, Donald W.: Clinical Considerations of Benign Ovarian Cystomas. Amer. J. Obst. & Gynec., **62**:806-817 (Oct.) 1951.
9. Montgomery, J. B.: Malignant Tumors of the Ovary. Amer. J. Obst. & Gynec., **55**:201-215, 1948.
10. Beacham, C. T.: Androgen Therapy in Pelvic Malignancy. Amer. J. Obst. & Gynec., **46**:849-852, 1943.
11. Taylor, H. C., Jr.: Ovarian Carcinoma. Meigs Progress Gynecology, Vol. 2. New York: Grune and Stratton, 1950.
12. Munnell, E. W.; and Taylor, H. C., Jr.: Ovarian Carcinoma. Amer. J. Obst. & Gynec., **58**:943-955, 1949.
13. Wheelock, Frank C.; Fennell, Robt. H., Jr.; and Meigs, Joe V.: Carcinoma of Ovary. New Eng. J. Med., **245**:447-459 (Sept. 20) 1951.
14. Walter, R. I.; Bachman, A. L.; and Harris, W.: The Treatment of Carcinoma of the Ovary. Am. J. Roentgenol., **45**: 403-413, 1941.
15. Crossen, H. S.: The Menace of "Silent" Ovarian Carcinoma. J.A.M.A., **119**:1485-1489 (Aug. 29) 1942.

DISCUSSION (*Abstract*)

Dr. Lee F. Turlington, Birmingham, Ala.—Dr. Guerriero made his first appearance before this section in 1929 when the Association met in Miami, at which

time he presented a paper on ovarian tumors. At that time he said that all ovarian tumors 5 cm. or more in diameter should be viewed with suspicion, and excepting those suspected of being follicular cysts the tumor should be removed as soon as found. Cysts that measured 5 to 7 cm. in diameter that did not disappear in four to six weeks should also be removed. This is about the same position he has taken today.

It is thought that a note of conservation should be introduced for the benefit of the young patients and the young and eager surgeons. Many follicular cysts reach the pathological laboratory! A test that has proved of advantage is the administration of estrogen in rather large doses to a patient who has a tender freely movable ovarian cyst of 5 to 7 cm. in diameter. After the patient takes 5 mg. of premarin® for fourteen days, many such cysts have been observed to disappear.

It is most important to have facilities at hand for frozen section diagnosis of ovarian tissue when it is suspected that a patient may have an ovarian tumor. Of course, every case is to be individualized but if a malignant tumor is found in one ovary, unless there is an extenuating circumstance, the other ovary, even though it appears normal, should be removed. This discussant cannot subscribe to the prophylactic removal of apparently normal ovaries between the ages of forty and fifty years.

The check-up examination every twelve months for patients under thirty-five years of age and every six months for those over thirty-five years cannot be too strongly emphasized.

Dr. John C. Weed, New Orleans, La.—Dr. Guerriero has made a vigorous plea for further consideration of the problem of ovarian carcinoma. Although ovarian carcinoma occurs less frequently than malignancies of the uterine fundus and cervix, it nevertheless has a high rate of inoperability and a low rate of survival, a fact which attests to the difficulty commonly experienced in establishing the diagnosis early and in effecting satisfactory treatment.

As Dr. Guerriero has emphasized, symptoms are conspicuously absent in the early stages of carcinoma of the ovary, and when they do appear they are referable to the gastro-intestinal tract or to the abdomen generally. Many patients with symptoms of abdominal swelling or ascites are first seen by internists. It has been a long and hard struggle at the Charity Hospital in New Orleans to keep the internists from performing abdominal paracentesis of large ovarian cysts, which may be malignant. By that time, however, the malignancy may have extended to the peritoneum. Few patients have pelvic symptoms in the early stages except those with functional tumors, such as granulosa cell tumors or arrhenoblastomas, which occur as a rule in younger women and upset the menstrual cycle.

In the training of every gynecologist it is important that he become familiar with the gross pathology of ovarian tumors. This can hardly be emphasized enough. Biopsy followed by immediate frozen section study is indicated in all suspicious ovarian lesions. Because ovarian malignancies are frequently bilateral, the opposite ovary should be carefully inspected in young women in whom conservation is important, with bisection to the hilar region and biopsy also of any suspicious area.

Another consideration in the surgical management of ovarian tumors is adequate abdominal exploration. Too frequently, we gynecologists are guilty of restricting ourselves only to our own particular field. Adequate exploration of the stomach, colon and adrenal areas will produce dividends to those who do this conscientiously. I have had the experience of finding two unsuspected adrenal neoplasms simply by palpating the upper part of the abdomen.

Finally, not only the medical profession but the female population as well must be made conscious of the dangers of ovarian malignancy. Whereas women willingly submit to examination for mammary or cervical tumors, few ever consider the possibility of ovarian tumors. Too frequently, they feel a false sense of security after the climacteric has been passed. Some of this is imparted by their professional advisers. It has been our custom for years to advise periodic examination of all women. Careful palpation of the adnexal regions of the pelvis should be incorporated into every such examination. Only by early detection can there be appreciable improvement in the operability rates and survival rates of ovarian carcinoma.

Dr. Guerriero (closing).—I wish to add a word of caution concerning the indiscriminate removal of ovarian tissue, but at the same time, to stress again to every practitioner of medicine that the mortality from ovarian carcinoma will be reduced only when ovarian tumors are found in their incipient stages.

This will require repeated vaginal examination of all patients, particularly those who are forty years of age, at regular intervals of six months. If we could encourage older people to accept six months periodic examinations as the pediatricians and obstetricians have encouraged their patients to accept periodic examinations, there is no doubt that the mortality from this entity would be reduced considerably since all ovarian tumors found after that age could necessarily be removed before spread or metastasis had occurred.

PUBLIC HEALTH ASPECTS OF HEART DISEASE*

By ALFRED W. HARRIS, M.D.†
Dallas, Texas

During the past decade, numerous advances have occurred in the diagnosis and treatment of cardiovascular disease. These advances have made necessary changes in certain aspects of the public health approach to this disease. Believing that simplification of public health procedures regarding some phases of this problem may lead to more efficient handling, I should like to discuss these

*Read in Section on Public Health, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

*From the Department of Medicine, Southwestern Medical College of the University of Texas, Dallas.

†Clinical Associate Professor of Medicine, Southwestern Medical College of the University of Texas, Dallas.

procedures. It is unnecessary to stress before this group the continuing importance of cardiovascular disease as a public health problem. You are all aware that diseases of the cardiovascular system cause more illness, loss of time, and deaths than any other group of diseases known to man. In 1951, of 1,481,000 deaths from all causes, 767,000 or 51.8 per cent of the total were attributable to diseases of the heart and circulation.

For purposes of clarification in terminology at the outset, let us accept the definition set forth by the New York Academy of Medicine that "public health" is: "the practical application of laboratory research, sanitary engineering, epidemiology and mass education toward safeguarding the country against disease." I should like to emphasize mass education. It then appears that preventive medicine is primarily concerned with the health problems of the individual. Let us not separate these two disciplines, but rather travel back and forth across the artificial boundaries.

While there are more than twenty types of heart disease capable of causing death, five principal types account for the large majority of fatalities. These include: congenital malformations, rheumatic heart disease, syphilitic heart disease, hypertension, and coronary arteriosclerosis. Other important states such as diphtheritic myocarditis, subacute bacterial endocarditis, nutritional deficiencies, and pericarditis, though important in any general consideration of the problem of heart disease, will not be considered here because they have now largely been brought under control. For purposes of this discussion, therefore, let us consider advances in only the first five conditions together with their public health aspects.

CONGENITAL MALFORMATIONS

Tremendous strides have been made in the past two decades in the recognition and treatment of congenital heart disease. These developmental deformities of the heart and great vessels are relatively uncommon causing 2 to 5 per cent of all heart disease. In years past for purpose of prognosis only cyanotic and noncyanotic types were distinguished. Now these groups must be broken down into finer subheadings, with reference to the possibility of surgical correction.

Since the epoch making work of Gross[1] we seek avidly for the presence of a patent ductus arteriosus. Similarly, coarctation of the aorta is now amenable to resection. Recently, the use of arterial grafts have made even large resections feasible. The persistence of a vascular ring causing displacement of the trachea and esophagus can be corrected by division of the smaller segment of the ring. Another main group that may be distinguished are those patients with the tetralogy of Fallot. This group of blue babies was the prime group offered new hope by the ingenious operation devised by Drs. Blalock and Taussig.[2] Another lesion is tricuspid atresia in which there is atresia of the tricuspid valve, absence of or defective right ventricle and some defect in the auricular septum. It is frequently associated with pulmonary stenosis and may be associated with complete transposition of the great vessels. These patients may be offered the same operation as those with tetralogy, providing there is pulmonary stenosis. Isolated pulmonic stenosis without ventricular septal defect has been tackled by the Brock operation of valvulotomy. To distinguish the proper patients for the Blalock procedure it soon became important to recognize those with Eisenmenger's complex wherein the pulmonary artery was enlarged or of normal size leading to fullness of the pulmonary conus and a hilar dance. These patients are most definitively separated by finding high pressures in the pulmonary artery by cardiac catheterization and by simultaneous visualization of the aorta and of a normal or enlarged pulmonary artery by angiocardiography. The Blalock procedure offers such patients nothing.

Only recently has it become important to go one step further and distinguish the subcategory of pulmonic stenosis with reversal of the interatrial shunt. These patients have cyanosis and right ventricular hypertrophy and thus mimic patients with the tetralogy. The Blalock operation not only fails to help those with reversed interatrial flow but may throw this group into right ventricular failure. After the new vessel becomes effective a good deal of aortic blood flow is shunted into the pulmonary artery leading to a subsequent rise in left atrial pressure. This results in a change in the direction of the shunt flow throwing a high load on the right ventricle and leading to failure. In tetralogy this sequence does not occur since an overriding aorta prevents the right ventricular pressure from becoming higher than the systemic. In this newly emphasized group of cases, the operation of pulmonic valvulotomy must be done.

At the present time efforts are being made to close septal defects, to improve the circulation in transposition of the great vessels, to alleviate the pulmonary blood flow in the Eisenmenger's complex, to correct anomalies of the venous return by transplantation of the pulmonary vein to the left auricle, and to cut the aortic stricture in aortic or subaortic stenosis.

It is obvious that these strides have been made through surgical ingenuity and boldness. It is likewise apparent that diagnostic measures can no longer rest in simply labeling patients as having congenital heart disease, cyanotic or noncyanotic. I have given only a few examples of why it is necessary to determine and identify with exactness, not only the major defects, but also the pathological physiology dependent upon such malformation. Unfortunately, to make such definitive diagnoses, the technics of cardiac catheterization and angiocardiography are necessary. These aids are so expensive and require such highly trained personnel that they are practicable only in the teaching centers. It is necessary that these centers be more evenly distributed throughout the country. Until such facilities can be provided many thousands of cases are likely to remain undiagnosed.

The preventive aspects of congenital heart disease should also be considered. In 1941, Gregg[3] in Sydney, Australia noted that an unusual number of patients with congenital cataracts were being seen. These frequently were associated with congenital heart disease. Reasoning that the etiology might be a toxic, infectious, or constitutional disturbance of the fetus, he determined that a certain stage of the pregnancies had coincided with the period of maximum intensity of a widespread epidemic of rubella in Australia. Gregg's studies are now well confirmed and it has been established that rubella and probably other virus diseases appearing in the first three months of pregnancy may lead to widespread delayed effects in the fetus. It has been established for many years that the period for the development of congenital cardiac defects is from the fifth to the eighth week of intrauterine life.

The question then arises as to the possibility of prevention of such anomalies both cardiac and extracardiac. Several courses are open to exploration. Aycock and Ingalls[4] suggest that inoculation with rubella may be a part of the pediatrician's future program of preventive medicine. At the present time our only positive approach is deliberate exposure before the childbearing age. Another aspect of the problem lies in the handling of the pregnant mother. Prophylactically immune globulins have been employed, but experience has not established their efficacy. It has been suggested that therapeutic abortion is indicated if rubella is contracted in the first two months of pregnancy.

RHEUMATIC HEART DISEASE

Recent advances in the treatment of rheumatic fever and rheumatic heart disease have not kept full pace with those in the congenital group. Swift pointed out that not only are statistics inadequate, but that the accuracy of diagnoses of both acute attacks and the sequelae or damaged hearts is extremely low. Although great strides have been made in our knowledge of the epidemiology of this disease since World War II, we have not taken full advantage of this increased information. Especially in the South, adequate facilities for the proper care and treatment for the afflicted are unavailable, even where accurate diagnosis has been made.

The mortality for rheumatic fever and rheumatic heart disease in a single year is almost double that for poliomyelitis for a whole decade. Yet adequate provision has been made for the care and treatment of poliomyelitis victims while almost no facilities are available for rheumatic fever patients. It should be pointed out that, while the diseases are similar in that there is a small proportion of fatalities in the early acute phase of each disease and both are crippling, a single attack of poliomyelitis confers almost complete immunity while an attack of rheumatic fever increases susceptibility to frequent recurrences.

There are, of course, adequate precedents to follow in the care of these rheumatic children. The London County Council's Rheumatism Scheme has been in operation since 1926.[5] It is based on two points: first, that rheumatic fever is a chronic infection and hence its victims should receive adequate chronic treatment; second, that the relapsing nature of rheumatic fever and the consequent heart disease demand supervision over many years. This certainly demands special units for the hospitalization of early cases. In 1926, 2 per cent of all school children in London were suffering from rheumatic heart disease in some form. In 1936, the incidence had fallen

to 0.8 per cent. This is an adequate demonstration of what organization and facilities can offer.

The experience in World War II cantonments revealed a relationship between hemolytic streptococcal illnesses and rheumatic fever, and emphasized that rheumatic fever was a respiratory disease, a contact disease, and a crowd disease. Coburn[6] and, more recently, Rammelkamp[7] have emphasized that rheumatic fever can be prevented in carefully controlled clinics, barracks, or institutional populations by the daily administration of either sulfadiazine or penicillin. Paul[8] has pointed out that the disease is more common in those areas where people tend to herd together because of long periods of inclement weather. The northern half of this country and the Rocky Mountain area represent these ideals.

Since the London experiment a few state-wide programs have been undertaken in this country, most notably that in New York State. In the development of these programs, emphasis has been placed first upon education which must be imparted to physicians, nurses, and medical social workers. High on the list is a plea for recognition of the fact that basically rheumatic fever stems from an infectious disease. Second is a plea for better diagnosis and third, the provision of care for those already suffering from the disease. If a program of public education is to be undertaken, therapeutic facilities must be provided simultaneously.

During the past three and one-half years, originating with the imaginative experiments of Glover and Bailey,[9] Harken[10], and Brock,[11] an attack has been made upon the sequela of rheumatic fever, mitral stenosis. This lesion with its fish mouth contracture leads to the mechanical blockage of blood flow from the left atrium resulting in left atrial enlargement and, finally, pulmonary artery hypertension. Subsequently, there occurs right ventricular hypertrophy and failure. By means of either the finger fracture technic or the use of the valvulotome, the area of stenosis is reduced and the mechanical handicap thus neutralized. Although the murmur often remains, nevertheless the hemodynamics are so relieved that pulmonary artery hypertension subsides to normal values and these patients can enjoy life at a virtually normal level without discomfort. The criteria for selection of the patients is still in a state of flux, but primarily the classical patients are those having practically pure mitral stenosis with very little mitral insufficiency, no left ventricular hypertrophy and preferably those with no associated aortic lesion. If there is aortic regurgitation it must not be full blown with a wide pulse pressure. Whereas originally auricular fibrillation was thought to be a deterrent, this is no longer true. It is important that the pulmonary artery hypertension be demonstrated to be due to the mechanical block and not due to congestive heart failure. It has already been shown that subjective relief alone should not be the measuring stick for the success of this operation.

I would emphasize that it is extremely important that cases be selected properly so that we may avoid the sad state of affairs that developed in the performance of sympathectomies in a conglomerate group of hypertensive subjects, because of poor selection of the original cases. In the latter instance, now some 20 years later, we are still debating indications, results, survival rates, physiological effects, and in the main, the operation has slowly come into question because poor selection of cases did not permit a controlled followup. It would indeed be shameful for an ingenious operation such as the commissurotomy to travel the same pathway merely because therapeutic enthusiasm leads to the selection of poor cases. One need hardly point out that proper selection is difficult and necessitates the use of special technics at times. Certainly public health demands that such facilities be widely scattered over the country.

SYPHILITIC HEART DISEASE

Fortunately, it is no longer necessary to discuss at length the problem of syphilitic heart disease, since the incidence of this illness is diminishing at an extremely rapid rate. Reasons for this happy state of affairs are not difficult to find. Public health methods have been very successful in ferreting out patients with early syphilis, and the efficacy of penicillin and other antibiotics in the treatment of early syphilis have made late lesions increasingly uncommon. This points out very clearly what can be accomplished once the technic of identifying proper cases has been reached, particularly with the assistance of trained social workers.

DEGENERATIVE DISEASES

In 1900, of the total population of the United States, 18 per cent were 45 years of age and

over. In 1940 this group had increased to 26.5 per cent and in 1950, was estimated to be 30 per cent of the entire population. This aging population accounts for much of the increase in the incidence of diabetes, cancer, and diseases of the heart and arteries. It is this last group of patients which constitutes the greatest potential public health problem today. This group usually spoken of as having degenerative heart disease includes both hypertensives and arteriosclerotics. While the rarer forms of hypertension can be identified and eliminated, the problem is with those patients with essential hypertension consisting of approximately 95 per cent of the group. These cannot be handled directly inasmuch as basic knowledge of the cause and cure of this condition is lacking. Edgar Allen has summed up the problem neatly:

"It would be desirable to begin this presentation with optimism and to conclude it with authoritative statements. Unfortunately, in the consideration of hypertension in the medical literature and in the light of our present knowledge there is too little fact and too much fancy, too little evidence and too much opinion, too little knowledge and too many questions."[12]

The experiments of Goldblatt[13] in 1933 led to a renewed interest in the study of hypertension. Goldblatt's studies seemed to indicate that hypertension was renal in origin. It was thought that through continued study, the fundamental mechanism could be elucidated and would lead to rational therapy. This happy culmination of the problem has not come to pass. Eighteen years later, there is still much doubt whether experimentally produced animal hypertension is identical with the human malady. Although certain morphologic features seem to co-exist, the life history and therapeutic effects are certainly not the same, and the renal concepts have yet to be proved. Since therapists have not been able to cure hypertension, a tendency has originated to attempt to show progress through statistical studies on changes in survival rates. Frequently, these studies are improperly controlled and based on inadequate samples. As a result, it is only in the past ten years that reviews such as those of Flaxman[14] and Perera[15] have changed our thoughts. Perera particularly has shown that the life history of hypertensives at various levels is a much longer one than has previously been supposed. In many instances, patients have lived from three to 34 years with average duration of about 20 years following the first discovery of hypertension. He also emphasizes that essential hypertension starts in the late twenties and the early thirties and rarely has its inception after the age of 48.

There has been recent revision of thinking on an even more important concept, although conclusive proof is not yet available. It has long been the concept that hypertension almost inevitably led into arteriosclerosis and atherosclerosis and in many instances it was considered to be causative. It is now becoming accepted that despite the fact that hypertension and arteriosclerosis or atherosclerosis are frequently considered as a cause of death, there are probably two disease processes involved. One is hypertension, the other is arteriolar disease. It is the arteriolar disease that causes death and disability. Because of the ease of sphygmomanometric measurements, the tendency has been to blame the symptoms of hypertension on the level of the blood pressure. Actually the correlation is very poor. Some authorities doubt that the reduction of blood pressure is ever beneficial. It is only in light of these recently crystallized facts that new therapeutic measures should be evaluated.

From the public health standpoint, these new concepts are especially important. For many years public education has emphasized the importance of blood pressure as a cause of death, but little in the way of therapeutic measures has been available. Patients have thus been led to false hopes through the medium of dietary fads such as the low salt routine, sympathectomy, and numerous medicinal agents. All of these measures were non-physiologically thought out, and yet were espoused by many authorities after too brief an evaluation. Such therapeutic misdemeanors only serve to confuse and to frustrate patients and to lead to more hypertension as their anxieties increase.

The problem of arteriosclerosis presents similar frustrating circumstances. Our recognition that the population is gradually aging has promoted increased interest in geriatric research, with the result that our knowledge of pathogenetic mechanisms is slowly increasing. Again unfortunately, the therapeutic enthusiasts have run ahead of the assembled facts. Recent studies have shown that by arteriosclerosis or aging one means only the loss of elasticity and tortuosity without embarrassing the lumen. According to Kellner[16] atherosclerosis impinges on the lumen and cuts down on the blood supply of the tissue

supplied by that vessel. Apparently the endothelium of the vessel is at first structurally intact, and macrophages empty their content of lipids into the lumen. Later, the lipids are able to permeate the endothelium. The association of such atherosclerotic processes with increases in various fractions of the serum lipids has been widely studied recently with frequently unwarranted conclusions. Such poorly controlled studies can serve only to separate us further from the truth. In the past six to nine months, a more sharply defined picture has emerged. It would seem that a very poor correlation exists between the cholesterol level and the atherosclerotic processes. Gertler and associates[17] aver that the ratio between cholesterol and phospholipids is the most significant index. Recently, Barr, Ross, and Eder[18] using Cohn's fractionation technics, have studied all of the fractions, but particularly the cholesterol fractions as they exist in the alpha and beta lipoproteins. They have analyzed statistically the occurrence of these lipoproteins in animals, human cord blood, healthy young males and females, older males and females, patients with diabetes, coronary disease, nephrosis, and in Kendall's atherosclerotic animals. As this case series becomes larger correlations become more and more impressive. Significantly, these authors feel that their data are indicative only and not determinative. They make no therapeutic claims. The work of Gofman,[19] although of interest, has thus far not been substantiated and to my knowledge work sheets have not been published. He has found that there is an increased number of Sf 12 to 20 particles in association with atherosclerotic processes. In addition, he thinks there might be some lesser correlation with larger particles, Sf 30 to Sf 100 particles. He makes it clear that lipotropic agents such as choline, inositol and methionine, all have no effect on the lipoprotein fraction. Graham,[20] a collaborator of Gofman, has shown that heparin appears to act as a catalytic agent in converting the serum lipoproteins from Sf 100 to smaller Sf molecules. This action of heparin is not based on its anticoagulability function. Even prior to the work of Gofman and of Morrison, low fat and low cholesterol diets have been widely employed as a therapeutic measure. These unpalatable, highly restricted diets add to the patient's discomfort and increase the titre of cardiac neurosis. A well-controlled study was carried out at the Goldwater Memorial Hospital, where 35 patients were studied on a virtually fat-free diet, following a six-week control period on 90 grams of fat. It was found there was a definite increase of the neutral fats while the patients were on a fat-free regime.[21] Samples of serum were also sent to Gofman's laboratory and in four of seven patients, there was noted a marked increase in the Sf 12 to 20 fraction while the patients were on the fat-free diet. From this and the isotopic studies of Stetten and Chaikoff it appears that the basic metabolic pattern of an individual is not based on dietary changes. Kendall quotes Gofman as saying that a diet with less than 25 grams of fat will result in a rise in neutral fats and an increase in Sf 12 to 20 particles, but that if the amount of fat is raised to 50 grams a day, both of these levels fall. It appears that these conflicting bits of data cannot be completely resolved at the present time. The various lipid fractions reported may be connected more directly with lipid transport in the body than with atherosclerotic processes in the various tissues *per se*.

Two new public health ventures are of especial interest. The Framingham study,[22] an epidemiological approach to heart disease, is especially oriented toward hypertension and arteriosclerosis. The aim is first to record in as full detail as possible, the characteristics of each individual which are considered relevant to the presence or absence, or the potential development of cardiovascular disease. Second, it was desired on the basis of this examination as a whole to classify the population studied into two groups: (1) Those with definite signs of arteriosclerotic or hypertensive cardiovascular disease, and (2) those apparently free of these diseases, who might be termed normals. The "normals" are the principal objects of interest in the study. They will be brought back biennially for a period which it is hoped will extend as long as twenty years. The age group from 30 through 59 were selected for study. Newer technical aids to cardiovascular diagnosis will be studied as a by-product of this investigation, for example: electrokymography, newer electrocardiographic leads and miniature chest films. It is hoped to sample 6,551 people. Dawber[23] says that he will consider 80 per cent cooperation as excellent. The first analysis will be available in the summer of 1952.

Simultaneously, a community heart demonstration program has been in existence at Newton, Massachusetts. The report of three years'

experience has just been published.[24] It was learned that prevention of rheumatic fever and subacute bacterial endocarditis can be applied in a practical way in a community; also that several hospital services can be carried over into the community. As a result, a group technic for weight reduction was developed. Group education for patients with congestive heart failure on a low sodium diet is being offered by nutritionists. Rheumatic fever prevention was instituted, consisting of a prophylactic schedule of 100,000 units of penicillin taken orally three times a day for patients with a history of a first attack of rheumatic fever within the past five years. A dosage of 1,000,000 units of penicillin is advised orally daily for ten days for the treatment of suspected streptococcal infections in members of rheumatic fever families. Free throat cultures and penicillin at cost price were made available to physicians by the Newton Health Department for members of rheumatic fever families.

It may seem peculiar that in a talk on public health aspects, much time has been devoted to recent advances in cardiovascular disease. I must confess this was done intentionally. As a cardiologist, there is very little new that I could offer such an audience in the public health field; however, there was a second purpose. If you will recall our definition of public health, there was a phrase "mass education toward safeguarding the community." For some time I have felt that we, as physicians and as public health officials, have done a great amount of harm, as well as good, with some of our mass education. Where therapeutic accomplishments are unknown and in conditions wherein the etiology is also unknown, I am not certain that we are helping particularly by shouting how often this illness causes death and disability before lay groups and in newspapers and popular magazines. Perhaps this type of mass education may be alibied by some as necessary for raising funds. I cannot wholly agree, for it would seem to me that an honest statement of facts without the emotional "whoopla" would accomplish the same purpose.

I believe there is an even more serious error of commission. This concerns the popularization and repetition of scientifically unproved methods and agents. For example, as has been reviewed above, although it would be a wonderful solution to the problem, the true facts are that the low sodium diet is of very little efficacy in the practical treatment of essential hypertension. In the few instances where it is efficacious it has been found that it must be carried out very rigidly, it is expensive, it is bothersome to the family, and soon promotes a very unhappy and weakened patient. What has not been popularized is that it may be harmful and particularly in elderly patients, may lead to damage, especially if it is carried out rigidly in conjunction with other procedures such as the use of mercurials. Yet what newspaper and what popular magazine has not spread the mass propaganda of its benefit? It is difficult for me to see why popularization of the true facts of the proper care of hypertension would not lead to better rapport, to better education and, in the long run, to better therapy. This last error has already occupied five years, and thus reveals how long it takes to get such bits of misinformation out of the literature. It will take many multiples of five years to withdraw this concept from physicians, social workers, and patient-to-patient gossip.

Virtually the same type of argument can be stated for the low fat diet. We are just beginning to see the espousal of this diet. It appears in public health handbooks, press releases, talks to the laity and in refresher courses at medical schools. Yet proof for this concept is certainly lacking and, as pointed out above, there is a tremendous hiatus between the established facts and the clinical use of such a diet. In fact, there just is not sufficient data to say that such a diet accomplishes what is wished. I would not try to be clairvoyant and say that some modification of this diet may not help, but what I am trying to emphasize is that I do not feel the facts at this time justify any popularization of such a regimen. Furthermore, we should understand that avitaminosis and profound cardiac neurosis must go hand in hand with the exhibition of such a diet.

There is needed a much more affirmative approach, namely the filling in of all the facilities not now present that will allow for more accurate diagnosis of the disorders in which advances have been made: the congenital group, rheumatic heart disease, syphilitic heart disease, bacterial endocarditis, thyroid heart disease, pericarditis and other curable forms of heart disease. The use of screening technics over more widespread areas, the establishment of medical centers

for diagnosis in areas where they could best serve the segments of the population, particularly in the southern and western sections of the country, where they are not available, would be helpful. In such centers, cardiac catheterization and angiocardiography, perhaps even ballistocardiography and electrokymography could be done. A rheumatic fever and congenital heart disease registry could be kept so that more accurate statistics could be formulated. It is the responsibility of the local medical profession to make such centers available. If these facilities are not provided locally, I am sorely afraid that they will be provided for by Federal funds.

BIBLIOGRAPHY

1. Gross, R. E.; and Hubbard, J. P.: Surgical Ligation of a Patent Ductus Arteriosus; Report of First Successful Case. J.A.M.A., **112**:729, 1939.
2. Blalock, A.; and Taussig, H. B.: The Surgical Treatment of Malformations of the Heart in which there is Pulmonary Stenosis or Pulmonary Atresia. J.A.M.A., **128**:189-202 (May 19) 1945.
3. Gregg, N. M.: Congenital Cataract Following German Measles in the Mother. Trans. Ophthal. Soc. Australia (1941), **3**:35, 1942.
4. Aycock, W. L.; and Ingalls, T. H.: Maternal Disease as a Principle in the Epidemiology of Congenital Anomalies. Amer. J. Med. Sciences, **212**:366 (Sept.) 1946.
5. Thornton, C. E.: The London Scheme for the Treatment and Supervision of Juvenile Rheumatism. Acta Rheumatol., **9**:10 (May) 1937.
6. Coburn, A. F.: The Prevention of Respiratory Tract Bacterial Infections. J.A.M.A., **126**:88, 1944.
7. Denny, F. W.; Wanamaker, L. W.; Brink, W. B.; Rammelkamp, C. H.; and Custer, E. A.: Prevention of Rheumatic Fever; Treatment of the Preceding Streptococcic Infection. J.A.M.A., **143**:151-153 (May 13) 1950.
8. Paul, J. R.: Public Health Aspects of Rheumatic Fever. Rhode Island Med. J., **28**:15 (Jan.) 1945.
9. Bailey, C. P.; Glover, R. P.; and O'Neill, T. J. E.: The Surgery of Mitral Stenosis. Presented at Meeting of Am. Assoc. for Thoracic Surg., New Orleans, La., March 29-31, 1949.
10. Harken, D. E.; Ellis, L. B.; Ware, P. F.; and Norman, L.: Surgical Treatment of Mitral Stenosis. New Eng. J. Med., **239**:801-809, 1948.
11. (a) Brock, R. C.: Pulmonary Valvulotomy for Relief of Congenital Pulmonary Stenosis. Brit. Med. J., **1**:1121, 1948. (b) Baker, C.; Brock, R. C.; and Campbell, M.: Valvulotomy for Mitral Stenosis: Report of Six Successful Cases. Brit. Med. J., **1**:1283 (June 3) 1950.
12. Allen, E. V.: Degenerative Diseases in Preventive Medicine in Modern Practice, p. 414. New York: Paul B. Hoeber, Inc., 1942.
13. Goldblatt, H.; Lynch, J.; Hanzal, R. F.; and Summerville, W. W.: Studies on Experimental Hypertension: I. Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia. J. Exper. Med., **59**:347, 1934.
14. Flaxman, N.: The Course of Hypertensive Heart Disease: I. Age of Onset, Development of Cardiac Insufficiency, Duration of Life, and Cause of Death. Ann. Int. Med., **10**:748 (Dec.) 1936.
15. Perera, G. A.: Diagnosis and Natural History of Hypertensive Vascular Disease. Amer. J. Med., **4**:416 (March) 1948.
16. Kellner, Aaron: Lipid Metabolism and Atherosclerosis. The Ludwig Kast Lecture. New York Academy of Medicine, Oct. 8, 1951.

DISCUSSION (*Abstract*)

Dr. Wm. S. Brumage, Austin, Tex.—Heart disease is our number one health problem from the standpoint of mortality. Dr. Harris has presented a logical and practical classification of the five principal types of cardiac disease. As we all know, much can be done in the field of preventive medicine toward elimination of congenital, rheumatic, and syphilitic heart disease. Syphilitic heart disease has been eliminated as a major public health problem during the past few years as a result of the efficacy of penicillin in the treatment of early syphilis. The increased incidence of hypertensive and arteriosclerotic heart disease is perhaps our most difficult problem at the present time.

An affirmative approach is needed if we hope to initiate an effective control program in the field of heart disease. Mass education is most important but of little value if facilities are not present to detect and treat early cases of heart disease. The use of screening technics in the detection of heart disease should be expanded only if follow-up facilities for the diagnosis and treatment are also present. It is truly the responsibility of the medical profession to provide such facilities since the family physician should be the key person in any heart disease control program.

TREATMENT OF MASS BURNS*

By B. W. Haynes, Jr., M.D.
Houston, Texas

On July 16, 1945, a new era was heralded by the detonation of the first atomic bomb near Alamogordo, New Mexico. Approximately three weeks later the tremendous power of this new weapon was demonstrated by its use on the Japanese cities of Hiroshima and Nagasaki. At Hiroshima over four square miles of the city was completely devastated, 66,000 people were dead or missing, and 69,000 were injured. At Nagasaki one and one-half square miles of the city were instantly destroyed and 39,000 persons were missing or dead and 25,000 additional were injured. The initial awe which followed the impact of these blows has since given way to a more calm consideration and a careful analysis of the facts concerning the explosion. Fear of the unknown has been replaced by understanding. On this basis, planning for the future can proceed with confidence and assurance of ultimate success.

Though this communication will deal primarily with the treatment of mass burns resulting from such a disaster, the over-all picture of injury must necessarily be briefly reviewed.

Elements of the Explosion Which Produce Injury.[1,2]—Following the detonation of the bomb, a tremendous wave of pressure is generated which produces a large area of blast

*Read in Section on Public Health, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

*From the Department of Surgery, Baylor University College of Medicine, Houston, Texas.

destruction. In addition, large quantities of radiation in the form of infrared, visible light, and ultraviolet rays are liberated plus some x-ray and gamma radiation (*Fig. 1*). The effective component of the bomb explosion which produces the heat waves lasts approximately three to five seconds and its effects may be felt in terms of burns of the flash type for two and one-half miles from the center of the burst. Ionizing radiation such as gamma rays are able to penetrate the atmosphere to a lesser extent and in all probability will constitute a considerably less hazard than thermal radiation. This statement is borne out by the experience at Hiroshima where ionizing radiations accounted for 15 per cent of the total deaths, whereas thermal burns were responsible for 40 per cent. Thus, it appears that from the standpoint of burn therapy, radiation effects as a complication will occur most commonly in those patients closest to the blast center and thus less likely to survive, and probably will not present a major problem.

A second type of thermal injury which will result is that due to secondary fires, namely, fires which are due primarily to the blast effect on gas mains, heaters, and so on. There are no reliable estimates of the relative numbers of flash and flame burns which might result. For practical purposes, this distinction may be academic, since the therapy of both types is quite similar. Combinations of both, no doubt, would be common as well.

Aside from the essential elements of the explosion, many local factors will influence the total effectiveness of the blast and thus the number of casualties which might result. For example, the atmospheric conditions are of considerable importance in that a mist or fog might well diminish the transmission of high energy radiation and thus diminish the number of casualties of the flash burn type. A flat terrain increases the effectiveness of all components of the bomb. The experience at Hiroshima indicates that concrete buildings offer substantial protection against the blast effect particularly if these buildings lie at some distance from the blast center. Thus, in any American city which contains a large number of permanent stone and steel structures the protection afforded by this type of construction might conceivably be quite

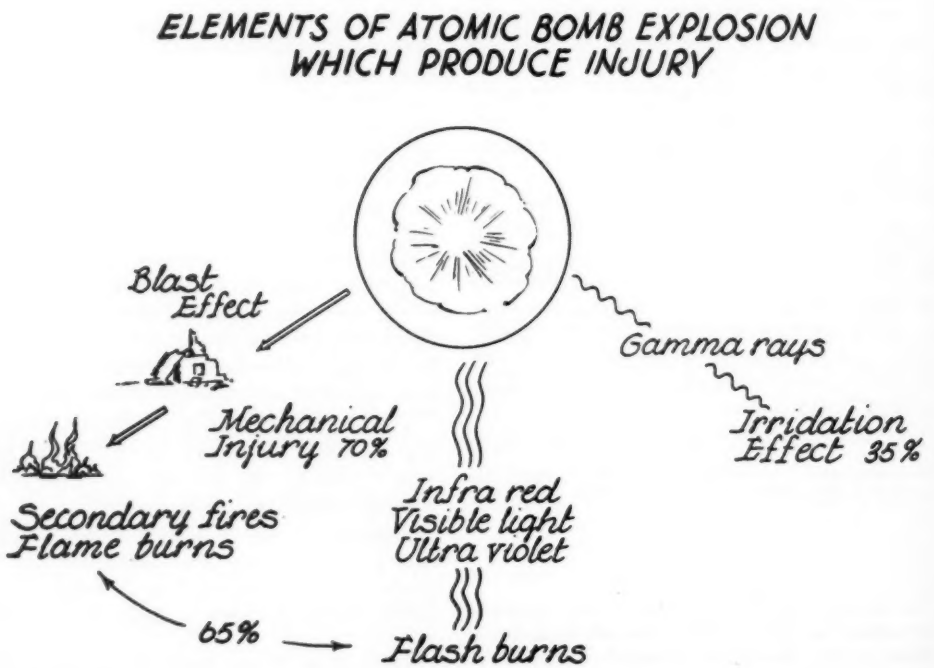


FIG. 1

This diagram shows the essential elements of an atomic explosion, their resultant effects, and the per cent of total casualties for which each was responsible based upon the Japanese experience.

significant. A further factor influencing the number of casualties is the time of day as it relates to the number of persons in a given area and whether or not these persons are out in the open.

It has been estimated that in an air burst explosion, 65 per cent of those persons exposed would suffer from thermal burns, 70 per cent from mechanical injury, and approximately 35 per cent from radiation to some degree. It is apparent that these injuries may or may not be in combination. It would seem to be a reliable estimate that of the 106,000 killed and wounded at Hiroshima, approximately two-thirds of this number suffered thermal burns of one type or another and of varying degree. Even though it would appear that certain factors previously mentioned which would operate in our own cities might markedly reduce the number of expected casualties in a city of similar size, planning must be geared to encompass the maximum number of casualties expected. Furthermore, the Hiroshima experience would indicate that of the total number of dead, thermal injury was responsible for 40 per cent, mechanical trauma for 45 per cent, and radiation for 15 per cent. It is well known that the burn therapy administered at Hiroshima was by any standard grossly inadequate.[11] Thus, of the approximate 70,000 dead there were 28,000 due to thermal injury as compared to the total of 70,000 burns received. There remained 42,000 people injured by burning who recovered for all intents and purposes spontaneously. It would seem, therefore, that approximately 60 per cent of the burn casualties will require minimal therapy to secure survival and, thus, efforts at burn treatment can be directed toward the group who died, relatively speaking, without effective therapy. Though in all probability this 28,000 dead represents combined injuries as well as thermal burns exceeding 40 per cent body surface area and, thus, quite difficult to treat successfully under optimum conditions, there was undoubtedly a substantial group of burns of lesser extent which would have responded had adequate therapy been delivered to them. With this background in mind let us now turn to an American city as an example and discuss the factors relating to the treatment of burn casualties under such conditions.

PATTERN OF DESTRUCTION[1 2]

In *Fig. 2*, we see a map of Houston depicting the areas of flash burn and secondary fires which might conceivably result from an explosion at the center of the city. This area was chosen as the site of the explosion to illustrate what might be expected to be the maximum bomb effect in terms of the numbers of burn casualties received. Should any of several industrial targets surrounding the city be chosen as the primary objective then the number of casualties would be less. However, because of the concentration of oil in these industries the secondary fire hazard would be greater than in a similar city of different industrial background. Extensive fire fighting equipment is obviously necessary. It is apparent from this figure that a good proportion of the available hospital space might be expected to be instantly destroyed or severely crippled. Power failure would hamper the effectiveness of any hospital remaining intact, and in addition, most units are already operating at capacity. It is probable that presently available hospital space will be of little use in the handling of mass burns.

It has been stated that destruction within the first one and one-half miles will be exceedingly heavy and it is unlikely that many persons will survive in this area. Should their burn component of injury be minimal it is probable that a combination of radiation plus mechanical trauma would be sufficient to produce a fatality. The greatest number of salvageable burns might be anticipated to occur in the area from one and one-half to two and one-half miles from the blast center. Burn injury, of course, may extend considerably beyond these limits.

With a few outstanding exceptions burn therapy is still conceived of today in terms of optimum care delivered under hospital conditions. It would seem apparent that a radical revision of these ideas is necessary to cope with the challenge of possible mass casualties. A particular effort must be directed toward simplification of therapy which has as its objective the offering of most good to the greatest number but, at the same time, is realistic in its approach. For example, it would be quite unwise to anticipate saving many deep second and third degree burns exceeding 40 per cent body surface area. Such an injury carries an exceedingly high mortality rate under optimum therapeutic conditions even today. It is also true that the effective treatment of mass burn injuries must inevitably depend upon effective evacuation. Though it is not within the scope of this discussion to go into the details of evacuation planning, it is clearly

recognized that this is essential and the effectiveness of this effort will largely control the effectiveness of burn treatment. To emphasize this interdependence, it is proposed to discuss the treatment of burns within the background of this essential counterpart, the evacuation of burn casualties.

TREATMENT AND EVACUATION

It would seem reasonable to anticipate that the most burn casualties would occur in the one and one-half to two and one-half mile range and intensive planning be directed toward evacuating this area. On the fringes of the city at distances perhaps three to four miles from the center, it would seem advisable to set up a series of clearing stations which would have as their purpose the sorting and treatment of casualties which would reach them by various means from the area of destruction (*Fig. 2*). From this point the more seriously wounded could then be evacuated to mobile hospitals placed a short distance from the outskirts of the city. This evacuation would be carried out by any type of transportation available and would require, to be effective, an extensive organizational effort. Casualties at the mobile hospital could be transferred to distant permanent hospitals by train, air, or car, for prolonged and definitive treatment. It is apparent at a glance that effective evacuation within the framework stated must be a community effort, that is, evacuation must be carried out to a great extent by the members of the community who are not injured or have received minor injuries as a result of the devastation. In this regard, an extensive teaching program explaining the anticipated lesser role to be played by ionizing radiation compared to thermal

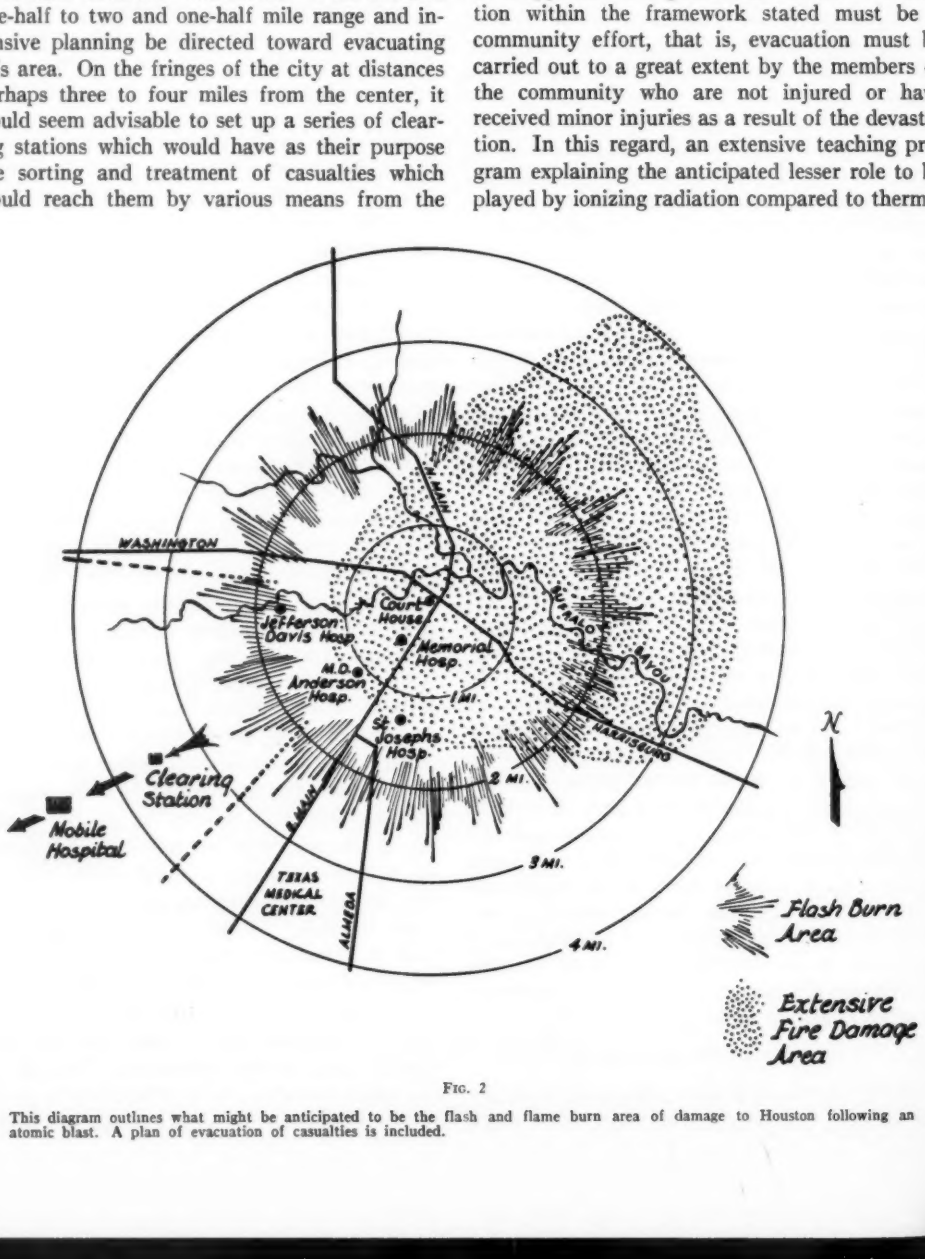


FIG. 2

This diagram outlines what might be anticipated to be the flash and flame burn area of damage to Houston following an atomic blast. A plan of evacuation of casualties is included.

burns following such an attack might lessen the degree of hysteria experienced. If hysteria is not well controlled, it might conceivably wreck any evacuation and treatment program. Increased emphasis on this point is of paramount importance. Within the area where most of the burn casualties can be anticipated, initial burn therapy must take the form of self-aid and will be dependent upon previous planning which will guide each individual in immediately seeking the nearest clearing station after injury. First aid administered for burns in this area will consist largely of hastening evacuation, and administration of morphine for the relief of severe pain. Experience has taught that one suffering a moderate burn uncomplicated by fracture or other trauma is still capable of walking for some distance. It would seem reasonable to assume that many burned patients might reach the clearing stations relatively unaided and not pose a major evacuation problem up to this point. A patient with extensive burns exceeding 40 per cent would be made as comfortable as possible, have his pain relieved by morphine, and his evacuation delayed in an effort to concentrate on those persons with lesser injuries and a greater chance of survival. It would seem impractical to deliver any more definitive measures of therapy closer to the area of explosion than the clearing stations.

The clearing stations should be set up as extensive centers which could process a large number of people in a short period of time. They would require staffing by physicians, nurses, and trained lay personnel. Such a center would provide facilities for removal of radiation contaminated clothing, cleansing of the skin of particles of radioactive contamination by repeated washing and donning some type of universal serviceable garment.[4] As a burn casualty presents himself to the station, a physician must first decide the extent of burn injury, and the nature of complicating wounds, if any. His examination must be necessarily physical in nature since laboratory facilities would not be available to any great extent. On his estimate must depend the recognition of minimal burns which will not require treatment beyond the clearing station level, and the choice of severely burned patients for evacuation, via ambulance or car, in order of probability of survival. Treatment at this level must accomplish, in order of importance: (1) relief of severe pain, (2) fluid replacement therapy, (3) antibiotic therapy, (4) therapy of the wound itself.

Relief of pain in the burn patient can be effected in one of two chief ways. Narcotics will, of course, accomplish this purpose. It can also be effectively combated by an occlusive dressing. In burns of lesser extent, simple application by the patient of petrolatum ointment will afford marked relief of pain. Under disaster conditions it would seem wisest to concentrate on relief of severe pain by means of morphine since the addition of dressings at this stage of evacuation would add a tremendous burden to available facilities and interfere with rapid evacuation. The dangers of the use of morphine in ambulatory patients are fully realized. It would seem practical, however, to assign each patient so treated to a second person who can assist in his evacuation. In the extensively burned patients who have had their clothing removed the problems of handling during evacuation make some type of dressing essential. It would seem, under these conditions, that Blocker's suggestion for the use of clean sheets to cover the burn wounds during evacuation would be practical and workable.[8]

Fluid replacement therapy at this evacuation level must consist primarily of oral therapy. Though several different salt combinations have been advocated for this purpose, the simplest and most effective substances would seem to be water and sodium chloride.[5] The use of a milk bottle or a pasteboard carton of water to which is added a slightly rounded teaspoonful of table salt would answer the requirements for a simple conveniently available oral therapeutic agent approximately isotonic with body fluids. Any patient with a severe burn should be encouraged to take in small amounts as much of this solution as he can tolerate. The danger of overdosage is minimal. The second aspect of fluid therapy will be confined to the intravenous use of plasma or plasma substitutes. The use of whole blood for this purpose in the quantities demanded would be entirely impractical. Evidence is accumulating which suggests that plasma substitutes are quite effective in the treatment of the early phases of burn injury and wound shock, and, while they cannot replace the red blood cell, they can effectively provide increased circulating blood volume.[9 10 14] They have the tremendous advantage that they can be stockpiled in almost unlimited quantity for use during an emergency. The severely burned patient could receive plasma

substitute therapy at the clearing station level. As a guide to fluid therapy, it would be well to display prominently on the walls of the clearing station a surface area chart. A simple and effective diagram is that of Wallace[7] which would give useful information. His "Rules of Nine" are easy to remember, and are reasonably accurate in both the child and the adult. It would appear that most burns of less than 20 per cent body surface area will recover with oral administration of fluid alone. The group of burned patients who have from 20-40 per cent surface area destruction will require plasma substitute therapy, and each individual in this severe burn category should receive 1,000 cc. of plasma substitute rapidly which in an average adult will constitute approximately one-half of his colloid requirement for the first twenty-four hours. He should subsequently receive a second 1,000 cc. of plasma substitute and should be instructed to take at least two milk bottles of salt solution in small amounts frequently and two milk bottles of plain water over the first twenty-four hour period after injury. Approximately two-thirds of this fluid intake total will be required during the second twenty-four hours. These fluid and salt amounts will meet the average requirement in the percentage area designated.* These instructions could be painted on the wall to insure their availability.

If he is not vomiting, the oral administration of a broad spectrum antibiotic can also be accomplished prior to evacuation from the clearing station. It would appear that the advantage gained from the use of an injectable antibiotic such as penicillin would not overcome the disadvantages of making such a preparation available on a large scale.

After the patient is evacuated to a mobile hospital on the periphery of the city, more definitive therapy can be delivered. A major portion of the facilities of this unit will be taken up with emergency surgical procedures and the beds required for this activity. A large number of beds must be set aside for the temporary hospitalization of burned patients, with emphasis on their further evacuation to permanent hospitals as soon as feasible. This unit would include most of the facilities of the modern hospital; whole blood must be made available here so that during or subsequent to the first forty-eight hours the deficit in red cell mass can be replaced. The most pressing problem will be determination of the adequacy of fluid replacement therapy. Vital to this determination is the measurement of the urinary output. Rates of 75-100 cc. per hour are optimal. A further check on the quantity of colloid and water that the patient has received must be carried out here and if the quantities previously designated have not been achieved or are inadequate, correction must be carried out at this level. Vomiting will pose a considerable problem in many of the patients demanding intravenous salt solution to meet the fluid requirements. It is probable that the treatment of the wound at this evacuation level must continue to be a simple covering with a clean sheet, since the major effort must be directed toward the more pressing problem of fluid replacement therapy. Facilities for administration of oral and injectable antibiotics must be available. Nutritional therapy must be simple and provision for high protein mixtures at this stage would not appear feasible.

As soon as evacuation facilities will permit, burn casualties of the salvageable group must be evacuated to a permanent hospital some distance from the scene of the destruction. Depending upon surrounding facilities and casualty load, patients may have to be transported hundreds of miles. Therapy during this transition must be largely fluid replacement in nature as well. Upon admission to a permanent hospital, definitive care more in keeping with the standards presently acceptable in our hospitals can be carried out. Decision as to the choice of optimum wound therapy is a debatable point. The closed dressing principle would seem to meet the requirements for the treatment of an open wound best under ideal circumstances.[12] It is feasible if this course is chosen to utilize a single dressing which can be mass produced and stockpiled, used either as a torso or as a limb dressing.[6] This can be applied with the usual pressure dressing technic. It would be unwise to bandage the hands prior to admission to a permanent installation, since this might reduce the in-

*These requirements are calculated on the basis of a 30 per cent body surface area burn, of a 70 kg. man, according to the formula advanced by Evans:[2]

70 kg. x 1 cc. colloid x 30 per cent burn	= 2100 cc.
70 kg. x 1 cc. salt and water x 30 per cent burn	= 2100 cc.
2000 cc. H_2O for urinary excretion	= 2000 cc.
	6200 cc. for first 24 hrs.

For the second twenty-four hours, one-half of the colloid and salt solution requirement, plus 2,000 cc. of water for urinary excretion will be required.

dividual's chance for survival. The use of the open treatment method has given good results in the hands of several observers.[7 13 15] Advocates of this form of therapy are enthusiastic. The chief advantage attributed to it, however, is better and more rapid wound healing with less infection and not the number of nursing hours saved. Thus, the choice of definitive wound therapy may take one of two well-defined courses. The closed method has been used extensively and to a large extent, satisfactorily. The open method offers considerable promise and may prove to be highly desirable.

In the permanent hospital, whole blood for the inevitable anemia which follows the severe burn must be the fluid replacement keynote. Adequacy of urinary output, of course, must continue to be evaluated. Attention to the correction of protein deficits by the use of a high protein diet such as that used by Evans[16] becomes practical at this stage of evacuation. Its importance does not need emphasis. Antibiotic therapy must be continued. The problem of tetanus immunization should be deferred until this level of evacuation has been reached. Ideally, teanus toxoid immunization of the entire population would constitute the most effective approach to the prevention of tetanus. Immunization by tetanus antitoxin in those who have not received toxoid would seem wise particularly in the contaminated burns with extensive destruction of tissue. A booster dose of toxoid will be required for those who have had previous active immunization. Further therapy of the wound, including skin grafting at an early date would be carried on at this installation.

SUMMARY

In conclusion, to be most effective the treatment of mass burns must be geared to an organized system of evacuation and temporary hospitalization and reduced to its simplest terms. In order for any treatment of burns on a mass basis to be effective a tremendous amount of organizational effort must have been achieved and directed toward removal of the injured in a systematic and orderly fashion. Herein it would appear lies the biggest job. Once this framework is assured, the minimum requirements for burn therapy outlined should not prove to be too difficult of achievement. It is, however, important that realism play a dominant role in burn therapy planning, recognizing on statistical grounds our inability to resuscitate the extensively burned patient so that planning will be directed toward those patients who will benefit most from the effort that we are able to deliver to the group as a whole. It is believed that the simple measures outlined for the treatment of severe burns can be made effective on a large scale basis and would result in a considerable saving of lives under disaster conditions.

BIBLIOGRAPHY

1. What You Should Know about the Atomic Bomb. The Surgeon General. U. S. Army Medical Dept., 1950.
2. The Effects of Atomic Weapons. Washington: U. S. Government Printing Office, 1950.
3. Purnell, O. J.; and Evans, E. I.: Electrolytes and Water. Symposium on Burns. National Research Council, Nov., 1950.
4. Lund, Charles C.: The Treatment of Burns after the Explosion of an Atomic Bomb. N. Y. Med., **6**:16, 1950.
5. Rosenthal, S. M.: Experimental Chemotherapy of Burns and Shock; Effects of Systemic Therapy on Early Mortality. Pub. Health Rep., **58**:513, 1943.
6. Allen, H. S.; quoted by Evans, E. I.: The Burn Problem in Atomic Warfare. J.A.M.A., **143**:1143, 1950.
7. Wallace, A. B.: The Exposure Treatment of Burns. Lancet, **1**:501, 1951.
8. Blocker, T. G., Jr.: Disaster Problems in Burn Care. Introduction. Symposium on Burns. National Research Council, Nov., 1950.
9. Evans, E. I.: Personal communication.
10. DeBakey, M. E.; Haynes, B. W., Jr.; and Amspacher, William H.: The Treatment of Wound Shock. Symposium on Shock. Army Medical Center Graduate School, May, 1951.
11. Evans, E. I.: The Burn Problem in Atomic Warfare. J.A.M.A., **143**:1143, 1950.
12. Haynes, B. W., Jr.: The Treatment of Thermal Burns of Small Extent. Surg. Clin. N. A., Oct., 1951.
13. Blocker, T. G., Jr.: Local and General Treatment of Acute Extensive Burns. The Open Air Regime. Lancet, **1**:498, 1951.
14. Thorsen, G.: Dextran. Symposium on Burns. National Research Council., Nov., 1950.
15. Pulaski, E. J.; Artz, C. P.; Shaeffer, J. R.; Huckabee, W. E.; Mitchell, R. C.; and Russell, J. P.: Exposure (Open) Treatment of Burns. U. S. Armed Forces Med. J., **2**:769, 1951.
16. Harkins, H. N.; Cope, O.; Evans, E. I.; Phillips, R. A.; and Richards, D. W., Jr.: The Fluid and Nutritional Therapy of Burns. J.A.M.A., **128**:475, 1945.

INDUSTRIAL HYGIENE PROBLEMS AS SEEN BY A WORKMAN COMPENSATION CARRIER*

By HENRY T. HERNDON†
Dallas, Texas

Interests in the control of industrial health has slowly progressed since the organization of the first Section on Industrial Hygiene at the American Public Health Association meeting in 1914.

The interests of those physicians in industries' health problems and the stimulus of the American Association of Industrial Physicians and Surgeons gradually increased the number of in-

---

*Read in Section on Industrial Medicine and Surgery, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

†Industrial Hygiene Engineer, Texas Employers' Insurance Association, Dallas, Texas.

dustrial doctors, although today a shortage exists in our Southwestern area. Should a greater number of specialists be trained or should our medical schools include in their undergraduate study an understanding of the ever-changing industrial processes, materials and exposures?

How many of our industrialists, their managers and superintendents, know or recognize the hurtful working environments in their own plants? In our contacts we are finding many who are extremely interested.

What shall be the approach in keeping abreast of the toxic limits of the constantly increasing number of new industrial materials? Shall we continue to use our biochemical instrument, the industrial worker, or shall we advise holding these new materials off the market until the safe limits have been experimentally determined?

I am sure we all agree that our standards for permissible atmospheric contaminants are helpful benchmarks, but what would you suggest to correct the gross misunderstanding of the so-called maximum allowable concentrations and threshold limit values?

Let us look into some of the Southern industrial plants.

In this primary heavy metal smelter the dryer mixer was installed with an open-end feed into the D & L hopper, and disperses large quantities of finely divided ore over the work area. Following some loss of productive employe time this was corrected by enclosing the feed.

In zinc smelting as well as a number of other metal smelters, electrostatic precipitator and collectors are used to collect valuable bi-products as well as toxic materials. In this smelter the precipitator employes daily dump the lead and cadmium concentrate onto the concrete floor below the electrostatic precipitator bin generating large quantities of dust. The dust is swept into piles and sacked by hand. The installation of a mechanical packer reduced this dust hazard as well as the labor costs.

Secondary lead smelting has its problems of atmospheric polution outside the plant as well as in. Metal and slag draws from blast furnaces contribute their share of fumes and an adequate exhaust hood connected to the smelter collecting system plays its part in reducing the contamination in the work area. Reverberatory furnace and refining pots are adding their oxide too, but adequate hoods whether stationary or portable help keep the concentration low. The boy charging battery scrap into the blast furnace feed is working in an atmosphere of less than 0.04 milligrams of lead per cubic meter while only a few feet away this worker pouring pigs with the metal around 630° F. was inhaling air containing 0.47 milligrams of lead per cubic meter. We found that the air currents were carrying the lead dust from this charging operation into the pouring operation work area. Wetting the scrap reduced this exposure below a toxic level. The handling of bagasse and manufacture of bagasse products with adequate collecting equipment and respiratory protection has added many manpower productive hours.

The industry of insecticide mixing has made itself well known to its neighbors as well as to the physician and insurance carrier with its atmospheric polution problems. Some material mixer layouts show no indication of industrial health engineering, some are designed with hoods for the protection of the plant personnel as well as conservation of materials.

The ancient industry of siliceous stone cutting has progressed in working tools and methods and some of the establishments have improved their present working conditions. This abrasive blast chamber removes the free silica from the work area and collects it in a wet collector thereby protecting the public as well as the employe. Some plants still persist in using a machine and hand surfacer without adequate exhaust and collecting equipment. Some exhaust their dust outside their plants onto the man next door.

Ceramics in modernizing their plants have not taken into account the control of process dust hazards. Open dry pans, open screens and open top storage bins are frequently found in this industry. Some companies continue to cut tile with no thought of protecting their workers.

The pickling of metal has its health hazards. Observe the hydrochloric acid and sulphuric acid vapor arising from these vats.

Galvanizing also generates vapors and fumes.

Asbestos carding, spinning, lapping, and weaving as well as moulded asbestos goods manufacture can and do incapacitate some of their productive personnel.

Lead oxide used on acid battery plates today may cause more trouble in the battery manufacturing business than any other substance. Oxide mixing, in the open and improper handling

and storage of pasted grids cast lead oxide in every nook and corner.

The chemical manufacturing and processing industries produce atmospheric contaminants too.

From the brass foundry comes the same old story "lead" whether melting, hand casting, or machine casting.

In the ferrous foundries we are still finding silica exposures in such operations as the shake out, grinding, and casting cleaning.

The American giant petroleum, mining, quarrying, steel, and all the rest contribute their part to our increasing industrial hygiene problems today.

DISCUSSION (*Abstract*)

Dr. Lewis William Fetzer, Dallas, Tex.—The paper by Mr. Herndon is replete with many descriptions of what is found commonly even now in industrial plants.

As far back as 1920, the American Chemical Society's Committee on O.D. paged the Public Health Schools, seeking the colleges who would train the superintendents and foremen in industrial hygiene, especially those in the more hazardous occupations. It also attempted to introduce Industrial Hygiene courses in all technical colleges who taught especially chemical engineering. Two institutions, Columbia and Harvard, and possibly two more, are giving this instruction as a regular feature, and my hope is that more will shortly fall in line. Unless we educate the foremen and superintending chemists along these particular lines, most of the effort spent in trying to eradicate these appalling conditions will be of no avail. Unless this is done an important link between the doctor and industrial hygienist, in trying to do something about it, is missing. In other words, the plant officials will be helpless and the doctor will not have a clear picture on what is transpiring in the first place.

Dr. Carl A. Nau, Galveston, Tex.—The speaker comes to us from an insurance carrier which carries many compensation insurance risks in Texas. He is the chief industrial hygiene engineer for his company which provides excellent engineering and analytical laboratory (mobile and stationary) facilities for him. He has intimate contact with and knowledge of industrial operations in Texas, and he is aware of many potential occupational health hazards and the control or elimination thereof. He has contact with many physicians and plant managers.

From the paper you have just heard, one can conclude that there is a need for more and better training of our physicians in industrial health problems; in industrial toxicology; and in the possible effects of working environment on health. Today, there are only 2,000 full-time industrial physicians in the nation. A mere handful of these are in Texas. About 75 per cent of the nation's workers are employed in 99 per cent of the nation's industrial plants that have 500 or less employes per plant.

A survey of our general practitioner of medicine reveals that over 80 per cent claim to do some industrial practice. In Texas, this figure probably is higher. Not many of these men ever had the opportunity as students to view industrial medicine beyond the realm of reparative surgery. While they were students in medical school, toxic materials, harmful environments, toxic limits, vapors, mists and gases with toxic properties, noise, vibrations, lighting, and so on, were not emphasized with sufficient force.

Today, as we rapidly become more industrialized, we see more clearly the need to emphasize these potential health hazards and others. We need to emphasize: (1) the importance of getting detailed occupational histories which will reveal the nature of the work done, materials exposed to, and final products made; (2) the possible relationship of the nature of the work, materials used, processes involved, environments created, and so on, to the health of the worker; and the effect of these same factors on the responsiveness to therapy and to recovery from non-occupational diseases.

Insurance carriers recognize the need for more physician interest in industrial medicine and for better opportunities for medical students and physicians to obtain specific training in this field.

The potential hazards our speaker referred to are only a few of the many he might have cited. He emphasized the interest of management. Any lack of interest usually arises from lack of information or wrong information. If management is to be more adequately informed, it is up to our physicians to do this informing. Every manager or owner of an industry has a family physician whom he consults and relies on, even for industrial health matters. If the industrialist is to be correctly advised and informed, it is necessary that his doctor have the necessary correct and basic information and a clear understanding of the philosophy of American business.

In the Medical Branch of the University of Texas at Galveston, we teach our undergraduate students the philosophy and concept of good industrial health and a few basic fundamentals as well. We hope other medical schools will do as much or more.

THE CLINICAL USE OF THE BARBITURATES*

By OLIVER F. BUSH, M.D.
Dallas, Texas

The use of drugs to produce varying degrees of sedation or hypnosis is one of the mainstays of the modern concept of psychosomatic therapy. Several types of drugs will produce sedation; of these the barbiturates comprise the largest and most important group. Of the several hun-

*Read in Section on Anesthesiology, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

dred barbiturates that have been prepared about twenty-five are in current clinical use. These drugs vary so widely in their actions that, in order to select the proper barbiturate for the purpose desired, it is necessary to be somewhat familiar with the pharmacological behavior of this group of drugs as a whole.

The most useful classification of barbiturates is based on their duration of action. In general, all barbiturates fall into one of four groups: the ultra-short acting, the short acting, the intermediate acting and the long acting. The ultra-short acting derivatives are characterized by an intense, rapidly induced hypnosis of short duration, whose peak of intensity occurs within a matter of seconds after intravenous administration. They are used principally in the production of anesthesia. Pentothal sodium,® evipal soluble® and surital sodium® are examples of this group. The short acting derivatives are characterized by a somewhat slower onset, less intense action, and a longer duration of hypnosis. In general the onset of action of this group occurs within a matter of minutes, the peak of intensity is reached in about one hour and the duration of action is seldom over three hours. Seconal sodium,® nembutal sodium,® amytal sodium,® delvinal sodium® and cyclopal sodium® fall into this group. The intermediate group is characterized by a less intense depression whose peak is gradually reached a number of hours after administration. They are used, mostly orally, when the hypnotic effect is desired several hours after administration. Ipral sodium® or calcium, dial,® alurate sodium,® and amytal® belong in this group. The long acting derivatives are characterized by a mild, gradually appearing, sustained depression. They are suitable when sedation without hypnosis is desired. Barbital, phenobarbital and phenobarbital sodium are the best known examples of this group.

The compounds within each group give essentially the same therapeutic effect; minor variations in pharmacological action have no clinical significance. The selection of the sodium salt or the free acid depends on the route of administration to be used and the rapidity of onset desired. The sodium salts are more soluble and have a more rapid onset of action than the free acid. Usually a slightly larger dose of the sodium salt is required to produce a given effect.

The barbiturates may be administered orally, rectally, subcutaneously, intramuscularly, intravenously or intrathecally. The oral route is the most commonly used. Here the desired effect is obtained through the choice of drug, dosage and the form in which it is administered (for example, elixir, tablet, capsule, coated capsule, and so on). Rectal administration in the form of suppositories or solutions is commonly used in children and adults in whom the oral route is inadvisable. Intramuscular injection is to be preferred over the subcutaneous route because of the alkalinity of the salts. The intravenous route should be reserved for the production of anesthesia or for those circumstances where an immediate effect is required. The intrathecal route has recently been investigated by Morrison, Koppanyi, and Tuohy.[1] They reported that certain barbiturates, when given intrathecally, will produce characteristic sensory anesthesia, varying degrees of motor anesthesia, and a prolonged central soporific effect.

Other factors which play a part in determining the choice of a barbiturate are the site of action and method of detoxification or elimination of the drug. A sedative dose of phenobarbital, for example, will produce a relatively greater depression of cortical activity than the other barbiturates, and is therefore more useful in preventing the *grand mal* convulsions of epilepsy. The other drugs act primarily on the hypothalamus, but all will produce a depression of the central nervous system from above downward as the dosage is increased.

The long acting group of drugs are eliminated principally unchanged in the urine. Their action is therefore prolonged unduly if renal damage exists. The short acting and ultra-short acting drugs are detoxified by the liver. They are therefore contraindicated if hepatic damage exists. The intermediate acting drugs are partly eliminated unchanged in the urine and partly destroyed by the liver.

Recent work by Brodie and his associates[2] has opened a new concept of the fate of the barbiturates in the body. Working with pentothal sodium® tagged with radioactive sulfur, they showed that most of the pentothal® administered was quickly deposited in fat depots throughout the body and, presumably, slowly released from these depots.

Since the clinical use of the barbiturates covers practically the entire field of medicine only a few specific examples will be mentioned here. The long acting barbiturates are indicated primarily when prolonged mild sedation is desired, as in hypertension, hyperthyroidism, heart failure and nervous tension. If, however, impaired renal function also exists, one of the intermediate acting compounds should be substituted.

The short acting compounds should be used where some degree of hypnosis is desired, as in obstetrics, insomnia, preparation for painful examination or preoperative preparation. Certain of these drugs are now available in preparations suitable for intravenous injection, and they are very useful in immediately controlling convulsions such as those resulting from overdosage of local anesthetic drugs, as hypnotic agents to supplement regional anesthesia, and as induction agents for inhalation anesthesia.

The ultra-short acting barbiturates are widely used for induction of anesthesia and for the maintenance of anesthesia in conjunction with one of the anesthetic gases. This type of anesthesia is contraindicated in patients with impaired liver function, chronic pulmonary disease with low vital capacity, marked anemia, shock, and respiratory obstruction. Recent work has indicated that caution should be used in administering pentothal sodium® to patients who have been receiving antabuse, as this drug prolongs the action of pentothal® in mice to 50 times normal.

As a further precaution the ultra-short acting drugs should be administered only by trained personnel and only when facilities for artificial respiration and administration of oxygen are immediately available.

Habituation to the barbiturates is now widespread, and this type of addiction resembles that of alcoholism and narcotic addiction in many respects. Treatment may be very difficult if the patient has been taking large amounts of barbiturates for any length of time. Almost all barbiturate addicts use the short acting drugs; therefore, in order to avoid the creation of new addicts, it is recommended that only the long acting drugs be prescribed if treatment over a prolonged interval is indicated. If the short acting drugs are used it is recommended that they be prescribed in small quantities and the indications for their use frequently reviewed.

Finally, the treatment of barbiturate overdosage must be briefly considered. Three principal reasons underlie most cases of barbiturate poisoning: first, those due to accidental ingestion, as by children; second, those due to suicidal attempts; and third, those due to the peculiar phenomenon of automatism, in which the patient, after taking a hypnotic dose, will sometimes get up and take repeated doses without being consciously aware of his actions. The prevention of these accidents is simple. Do not allow the patient to have access to large quantities of barbiturates at any time. The treatment may be outlined as follows:

(1) Establish a clear airway and ensure adequate oxygenation. Pharyngeal airways or endotracheal tubes may be used. A tracheotomy should be performed without delay if these are not available or satisfactory.

(2) Gastric lavage with an alkaline solution. This is most helpful if it can be done within a few hours after the drug has been ingested.

(3) Maintain normal physiologic function as nearly as possible through proper intravenous therapy, conservation of body heat, frequent changes of position, and so on.

(4) Administration of stimulant drugs. In mild cases ephedrine, caffeine and sodium benzoate or benzedrine may be sufficient. In cases severe enough to cause loss of reflexes the cautious intravenous administration of picrotoxin until reflexes return is preferred. Metrazol® is an effective stimulant, but its action is so transient that it is best to confine its use to test doses to determine the depth of depression.

(5) Antibiotic therapy, in anticipation of the pneumonia that very frequently develops in these patients.

Treatment may have to be continued for several days. The ultimate prognosis depends more on the rapidity with which adequate treatment is instituted and the care with which it is administered than on the total dose of drug ingested.

BIBLIOGRAPHY

1. Morrison, R. L.; Koppanyi, T.; and Tuohy, E. B.: The Spinal Anesthetic Effects of Barbiturates: Preliminary Report. J. Anesthesiology, **12**:315-320, 1951.
2. Brodie, B. B.; Mark, L. C.; Papper, E. M.; Lief, P. A.; Berstein, E. and Rovenstein, E. A.: The Fate of Thiopental in Man and a Method for Its Estimation in Biological Material. J. Pharmacol. and Exper. Therap., **98**:85, 1950.
3. Giarman, N. J.; Flick, F. H.; and White, J. M.: Prolongation of Thiopental Anesthesia in the Mouse by Premedication with Tetraethylthiuram Disulfide ("Antabuse"). Science, **114**:35, 1951.

CORTISONE IN ACUTE RHEUMATIC CARDITIS*

By JOHN A. BOONE, A.M., M.D.†
and
MYLNOR W. BEACH, M.D.‡
Charleston, South Carolina

Because of current widespread interest in the treatment of the varied manifestations of rheumatic fever with cortisone and ACTH, it was felt worthwhile to report our experiences with one of these drugs in a small series of six patients, most of them severely ill. Previous work has been summarized by Harris and others,[1] and in general these reports have been favorable. Most of our cases were of such severity that more than the previously available therapy was indicated, and it appeared to us an excellent opportunity for this drug to demonstrate its usefulness. Despite other favorable reports, we were unable to demonstrate that it was clearly of benefit in any of our six patients.

CASE REPORTS

Case 88,000.—A Negro girl was found at birth in 1934 to have a positive Wassermann reaction. Antisyphilitic treatment was sporadically given during the first year and again for a short time in 1939, when the tonsils and adenoids were removed because of repeated sore throats. At this time a soft systolic murmur in the aortic area was heard but no rheumatic history was obtained. She was next seen in February, 1950, at the age of 16 complaining of fever, abdominal pain and a vaginal discharge. Neisserian organisms were found and her symptoms subsided under penicillin. The Wassermann reaction was negative on this occasion. The heart was found at the upper limit of normal size with a grade 3 systolic murmur at the apex. The sedimentation rate and electrocardiogram were normal. Again no rheumatic history was given. After discharge she continued to run a low grade fever and was readmitted one month later for study. Repeated blood cultures were negative. A sedimentation rate of 19 mm. per hour (Wintrobe) was found and rheumatic activity suspected. In September, 1950, she complained of palpitation, substernal pain, fever, anorexia and vomiting, but no joint pain. She did not return to the clinic until one month later, complaining of the same symptoms plus dyspnea and orthopnea. Examination showed a poorly developed, weak, sick-looking girl, slightly dyspneic and orthopneic. The temperature was 101.2° F., the blood pressure 140/50. The heart beat was rapid and regular at a rate of 130. A harsh systolic murmur and a grating friction rub were heard maximally at the apex. The lungs were clear, no abdominal organs were palpable and no edema or venous distension was obvious. The blood showed a red cell count of 3.3 million, hemoglobin 9 gm. per 100 cc., white cell count 12,000 with a normal differential. The blood sedimentation rate (Wintrobe) was 24 mm. per hour. The urinalysis showed no abnormalities and good concentration. Symptomatic treatment only was given for two days. On the third day 200 mg. cortisone was given, followed by 100 mg. daily for 12 days, a total of 1.4 grams. The temperature became normal on the fourth day but the patient's general condition progressed steadily downhill. The friction rub persisted and on the fifteenth day it was felt that a pericardial effusion had developed. A pericardial paracentesis yielded no fluid, and death finally occurred one hour later. Autopsy showed 300 cc. of fluid in the pericardium and a large amount of shaggy fibrinous material covering the entire heart surface. Verrucous vegetations were present on all valve margins except the pulmonic. Sections of the heart muscle showed fragmentation, many Anitschkow cells and a few poorly developed Aschoff nodules.

Case 95,857.—A white boy, 18 years of age, was admitted to Roper Hospital, December 14, 1950. Three months before he had developed hot, swollen, painful joints and fever. Remissions and exacerbations of these symptoms had persisted since then and he lost 14 pounds in weight. On admission the temperature was 99° F. and no joint involvement was noted. The heart was rapid and regular at 130 per minute and appeared at the upper limit of normal in size. A harsh grade 3 systolic murmur was heard at the apex and over a wide area of the precordium. The electrocardiogram showed a P-R interval of 0.20 second. The white blood count was 16,600 with 83 per cent polymorphonuclears. The corrected blood sedimentation rate (Wintrobe) was 26 mm. per hour. The day after admission he was given 300 mg. cortisone, the third day 200 mg., and 100 mg. daily thereafter for 10 days. After the third day the pulse rate remained between 90 and 100 per minute, but the temperature showed no change and the blood sedimentation rate was 23 mm. per hour on the sixth day and 19 mm. per hour on the ninth day. Cortisone was discontinued on the tenth day and he was discharged to remain in bed at home.

Case 56,068.—A white girl, 11 years of age, was admitted to Roper Hospital, December 14, 1950. At the age of six she had her first bout of rheumatic fever and since then had several hospital admissions for recurrences, including one year spent in a convalescent hospital. Three weeks previously she became ill with painful ankles and knees and fever which had continued until admission. The previous day scattered itching wheals had appeared over the skin. Examination showed an acutely ill child with temperature of 100° F. The apex of the heart was palpable in the left anterior axillary line and was regular

*Received for publication October 10, 1951.

*From the Departments of Medicine and Pediatrics, Medical College of South Carolina, and the Medical and Pediatric Services, Roper Hospital, Charleston, South Carolina.

†Professor of Medicine, Medical College of South Carolina.

‡Professor of Pediatrics, Medical College of South Carolina.

at a rate of 170 per minute. A loud harsh systolic murmur and a gallop rhythm were heard at the apex and there was a pericardial friction rub in the third left intercostal space near the sternum. The liver was palpable two fingerbreadths below the right costal margin. The lungs were clear and there was no edema. The blood showed a red cell count of 3.4 million, a white count of 5,700 and a hemoglobin of 9 grams per 100 cc. The blood sedimentation rate (Wintrobe) was 28 mm. per hour. A blood culture was negative. Treatment was begun with procaine penicillin 300,000 units three times daily, and sodium salicylate 10 grains with ascorbic acid 100 mg. every four hours. By the third day the patient seemed more ill and listless, and a transfusion of 250 cc. of whole blood was given. On the fourth day her condition was worse, difficulty with the respiration appeared, the friction rub was louder and the liver edge was palpable four fingerbreadths although the lungs still appeared clear. Salicylates were discontinued, another 250 cc. transfusion was given, and cortisone, 100 mg. daily was begun. During this day she began coughing up small amounts of frothy material with a few streaks of bright blood. On the sixth day she was dyspneic, slightly cyanotic, the neck veins were distended, the lungs full of coarse rales and rhonchi and the liver a full handsbreadth palpable. The friction rub and murmurs were unchanged, and the patient was obviously worse. Administration of oxygen by nasal catheter was begun. The general condition was unchanged on the seventh day and she was placed in an oxygen tent. On the eighth day she was worse, more cyanotic and edema for the first time appeared in the eyelids and extremities. Thiomerin 1 cc. was given subcutaneously and streptomycin, 0.5 gram three times daily was begun. At 4 a.m. on the ninth day, immediately after being given her oral medication, she vomited and ceased to breathe. Autopsy was not obtained.

Case 95,910.—A colored girl, nine years of age, when two years old had a very severe sore throat with high fever. Bouts of fever during the summers of the two following years were treated as malaria. At the age of five years, fever and multiple joint involvement occurred, a diagnosis of rheumatic fever was made and she was kept in bed for six months. Recurrent attacks of fever and joint pain had occurred each winter since then. Recently edema of the feet was noted. Two weeks before admission, her latest attack had begun and she entered the hospital January 11, 1951. Examination showed a chronically ill child with pallor of mucous membranes, a heart with apex beat in the anterior axillary line, regular at 160 per minute with a harsh apical systolic murmur and a liver palpable 4 cm. below the right costal margin. There was no joint tenderness or evident edema. The temperature was 101° F. The blood sedimentation rate (Wintrobe) was 34 mm. per hour, the red cell count was 3.3 million, the hemoglobin 8 grams per 100 cc., the white cells 17,500 with 90 per cent polymorphonuclears. A blood culture showed no growth. Treatment was begun with sodium salicylate 10 grains every four hours, ascorbic acid 100 mg. three times a day and cortisone, 38 mg. daily. The following day chloramphenicol, 200 mg. four times daily was begun. The patient appeared to do well. By the morning of the third day the temperature had become normal though the pulse rate continued between 120 and 140 per minute. That afternoon the respirations became quite rapid and salicylate was discontinued. On the fourth day oxygen by nasal catheter was begun, but with little effect on the rapid respiration. By this time the temperature had risen to 102° F. At this point digitalization was begun and the following (fifth) day the salicylate dosage was restored. By the seventh day the temperature had dropped to 100° F., the respiration was slower and because of general improvement, oxygen therapy was stopped. On the eighth day, respiration again appeared rapid and difficult and oxygen therapy was reinstituted. She vomited several times that night and on the ninth day appeared quite restless and apprehensive. Salicylates were again discontinued. The general condition continued to deteriorate and both pulse and respiration ceased at midnight. Autopsy was not obtained.

Case 86,944.—A white girl, 13 years of age, had been well until 18 months previously when she had an episode of fever and pain in the legs which lasted nine days and was diagnosed malaria by her family physician. One month after this one ankle was swollen and painful for several days. Following this she developed a lumpy rash (erythema nodosum?) on the legs which lasted for two to three months. One year before admission a physician diagnosed "rheumatic fever and a bad heart" but allowed her to attend school. Two months later she developed dyspnea and generalized edema, spent several weeks in the hospital and then two months in bed at home. On gradually increasing activity her dyspnea and edema recurred and after eleven more days in a hospital she improved. She remained apparently in good health until three weeks before admission when edema and a persistent cough appeared and increased in severity.

Physical examination showed generalized edema, slight dyspnea and ascites. The heart was enlarged to the left anterior axillary line. The rhythm was regular and rapid. A harsh systolic murmur and thrill were present at the apex and a faint early diastolic blowing murmur was heard down the left sternal border. There were signs of fluid at both lung bases. The liver edge was palpable a full handsbreadth below the right costal margin and there was a protuberant abdomen with shifting dullness and a fluid wave. Both legs showed 3 plus edema to the knees. The blood pressure was 140/70. Laboratory studies showed a normal blood cell picture. The blood sedimentation rate (Wintrobe) was 28 mm. per hour on admission, rising later to 42 mm. per hour. The urine consistently showed high concentration, 4 plus albumin and varying numbers of pus cells. Numerous blood cultures showed no growth.

She was digitalized on admission and put on a low salt diet with limited fluids. The edema continued increasing and 12 days after admission cortisone was begun in doses of 125 mg. daily in divided doses and continued for ten days. No improvement, but a steady downhill trend was observed, and in addition a small amount of acne present on admission increased markedly. After discontinuing cortisone, repeated abdominal para-

centeses and mercurial diuresis achieved almost complete disappearance of the edema, but the patient continued to lose ground and became more dyspneic. A loud pericardial friction rub appeared one week before death, which occurred coincident with a sudden hyperpyrexia approximately four months after admission.

Case 57,348.—An eight-year-old colored boy was first at Roper Hospital in 1947 when he was hospitalized with what was thought to be acute rheumatic fever. At that time symptoms were fever, sore throat, peri-umbilical pain, and anorexia. The only pertinent finding was a grade 2 systolic murmur heard best at the apex. He remained essentially well afterward until December, 1950, when he was again admitted complaining of palpitation, fever, sore throat, nose bleed, and headache. He never had joint pains and the only interim symptom was occasional epistaxis. He was next admitted in December, 1950, complaining of fever and weakness for one week. Physical examination revealed an acutely ill young colored boy with a temperature of 104.° The blood pressure was 140/40. The heart was enlarged to the left with a grade 3 apical systolic murmur, a grade 3 aortic systolic murmur, and a grade 2 soft, blowing long diastolic murmur loudest in the third left intercostal space.

Laboratory findings revealed a white blood count of 9,500, hemoglobin of 12 grams. The blood sedimentation rate (Wintrobe) on December 24 was 10 mm. per hour while on December 27 it was 30 mm. per hour. It was felt that the patient had acute rheumatic fever with rheumatic myocarditis and he was given cortisone 50 mg. every four hours for six doses, 50 mg. every six hours for four more doses and then 25 mg. every six hours. During the next 24 hours he remained extremely ill and his temperature rose to 105.4.° Penicillin, 200,000 units every two hours, was given and over the next 24 hours the temperature dropped to 101,° and the patient was somewhat improved. Because of confusion as to the therapeutic response, cortisone was stopped about 60 hours after it was begun. The temperature remained at 101° for three more days and then dropped sharply with onset of salicylate therapy. He subsequently remained afebrile and totally asymptomatic and was discharged five weeks after admission.

One month later the patient reported to the emergency room again with similar acute symptoms and a temperature of 105.° He was given salicylates and penicillin over the next three days with no response. Multiple blood cultures had been drawn and because subacute bacterial endocarditis was suspected, penicillin was increased to one million units every two hours and sulfadiazine was begun in a dosage of one gram every four hours on the morning of the fourth day. That evening cortisone was begun at 50 mg. every four hours and by the next morning the patient was markedly improved with the temperature down to 99.5.° A pericardial friction rub which had been noted on the morning that cortisone was started persisted throughout the next day but was practically gone by the second day. Serial electrocardiograms were consistent with changes expected in acute pericarditis. Cortisone was gradually decreased to 50 mg. twice a day and further gradually decreased to 25 mg. daily, finally being stopped two weeks after it was begun. While the patient was on cortisone his temperature was normal for five days and gradually rose over the next four or five days to 104° F. on the day that cortisone was discontinued. During this time he appeared extremely ill with marked cardiomegaly, generalized edema, tachycardia, pleural effusion, ascites, and extreme prostration. The electrocardiogram remained abnormal with development of the typical picture of left heart strain. Over the next few weeks, however, he gradually improved with only an occasional temperature spike to 101° F. and increased well-being. He had been entirely afebrile for 17 days when persistent temperature elevation to 103° and 104° again appeared. On the sixth day of this spiking temperature reaction cortisone was restarted but five days later it was again stopped since no therapeutic response had been noted. Multiple blood cultures had always been negative but on the thirteenth day of this most recent temperature elevation, six cultures were returned all positive for Salmonella typhosa. He was then given chloramphenicol and five days later his temperature reached normal to remain so for the next three weeks. At the time this is written the patient is completely afebrile and entirely asymptomatic.

Examination of the heart continues to reveal marked aortic and mitral insufficiency. The heart is much smaller though still markedly enlarged. The electrocardiogram continues to show typical left heart strain.

It is felt that this patient definitely had acute rheumatic fever with rheumatic myocarditis. Response to cortisone on the first two occasions was masked by other drugs. However, it is clear that the patient had a flare-up of acute rheumatic fever while he was on cortisone. The third sustained temperature elevation was evidently due to a blood stream infection with Salmonella typhosa and cortisone was clearly not effective here. Chloramphenicol produced a prompt and effective response.

SUMMARY

Cortisone was given to six severely ill patients with rheumatic carditis. In two cases the dosage was probably inadequate, and in no case was the drug employed longer than 12 days. Four deaths occurred. In five cases, no evident improvement resulted. In one case, apparent improvement while on adequate dosage was followed by another flare-up of carditis while the patient was still receiving the drug.

REFERENCE

1. Harris, T. N.; Abrams, W. B.; Leo, T. P. F.; and Hubbard, J. P.: Cortisone Therapy in Acute Rheumatic Carditis: Preliminary Observations. Circulation, 3:215, 1951.

PERNICIOUS ANEMIA COMPLICATED BY ACUTE GRANULOCYTIC LEUKEMIA*

A CASE REPORT

By R. W. TALLEY, M.D.,
J. E. DOHERTY, M.D.
and
C. F. SHUKERS, M.D.
Little Rock, Arkansas

The development of granulocytic leukemia terminally in an elderly white man who had received treatment for pernicious anemia irregularly over a period of several years is reported. The coexistence of these two diseases is quite rare. The diagnosis of both diseases was well established in this patient.

CASE REPORT

J. F. D., a 65-year-old white man, a farmer, was first admitted to the University Hospital on March 6, 1946. He had a total of six admissions between March 6, 1946 and July 18, 1950.

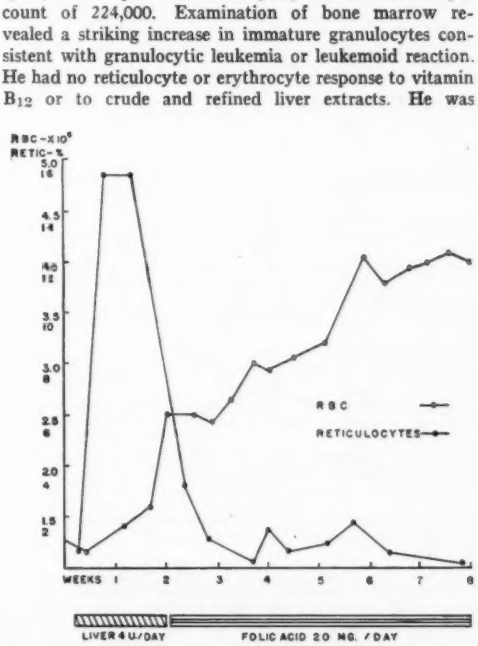
On March 6, 1946, he was admitted complaining of progressive weakness, dyspnea on exertion, and swelling of his feet and ankles of about five months duration. He had experienced anorexia and a 30-pound weight loss during this interval. Physical examination revealed a well-developed, well-nourished white man with sparse gray hair, blue eyes, and a waxy pallor of the skin. The tongue was beefy red and slick, the knee and ankle jerks were hypoactive, and there were diminished vibratory sensations over the ankle malleoli.

The laboratory findings were as follows: hemoglobin 5.96 grams; red blood cells 1.79 x 10^6; white cells 4,000 (*Fig. 1*) with 1 per cent eosinophils, 37 per cent segmented neutrophils, 58 per cent lymphocytes, and 4 per cent monocytes; titration of gastric secretion with histamine stimulation revealed no free hydrochloric acid.

A diagnosis of pernicious anemia was made and the patient was given four units of liver extract intramuscularly daily. There was a rise in the reticulocyte count to 15.6 per cent on the seventh day of treatment. On the fourteenth day of hospitalization, the liver extract was discontinued and the patient was given 20 mg. of pteroylglutamic acid orally. There was a gradual rise of the erythrocyte count to 4.2 x 10^6 and the hemoglobin rose to 12.5 grams per 100 ml. There was a complete disappearance of symptoms and signs over an eight-week period.

The patient was readmitted to the hospital on April 6, 1947, March 19, 1948, and January 4, 1950, in relapse. Each time he gave a history of having stopped taking liver extract two to three months previously because he felt so well. On each of these admissions, he complained of numbness and tingling of the feet and ankles. In all three admissions he responded well to liver extract with similar reticulocyte and erythrocyte responses as on the first admission (*Figs. 2, 3* and *4*). Bone marrow aspiration on March 19, 1948 (second admission) revealed a maturation arrest with marked increase of prorubricytes of pernicious anemia type. In January, 1950 (fourth admission) he was given liver extract, 10 units daily for two weeks. He was then placed on 30 micrograms of B_{12} every week. However, on this admission, he had a white blood cell count of 15,510 with 12 per cent myelocytes, 15 per cent metamyelocytes, 23 per cent bands, 29 per cent segmented neutrophils, 18 per cent lymphocytes, and 3 monocytes. Examination of bone marrow five days after initiation of liver therapy revealed a normal bone marrow. The leukocyte count two weeks after initiation of therapy was 5,250 with 4 per cent eosinophils, 7 per cent myelocytes, 9 per cent metamyelocytes, 49 per cent bands, 29 per cent segmented neutrophils, and 2 per cent lymphocytes.

The patient was readmitted on May 24, 1950 for the fifth time complaining of severe weakness and precordial pain on exertion. He had taken the vitamin B_{12} as directed during the interval since the last hospitalization. The erythrocyte count was 2.28 x 10^6, the leukocyte count was 24,900 with 1 per cent basophils, 1 per cent eosinophils, 3 per cent myeloblasts, 18 per cent myelocytes, 30 per cent metamyelocytes, 13 per cent bands, 20 per cent segmented neutrophils, 12 per cent lymphocytes, and 2 per cent monocytes, and a thrombocyte count of 224,000. Examination of bone marrow revealed a striking increase in immature granulocytes consistent with granulocytic leukemia or leukemoid reaction. He had no reticulocyte or erythrocyte response to vitamin B_{12} or to crude and refined liver extracts. He was



FIRST ADMISSION

FIG. 1

*Received for publication January 12, 1952.

*From the Departments of Medicine and Clinical Pathology, University of Arkansas School of Medicine, Little Rock, Arkansas.

*Nomenclature used as recommended by the Committee for Classification of the Nomenclature of Cells and Diseases of the Blood-Forming Organs: First report, Am. J. of Clin. Path., 18:443 (May) 1948; Second report, Am. J. of Clin. Path., 19:56 (Jan.) 1949; Third, Fourth, and Fifth reports, Am. J. of Clin. Path., 20:562 (June) 1950.

given 1,500 cc. of blood during this admission (*Fig. 4*). At the time of discharge one month after admission, there was no change in the white count.

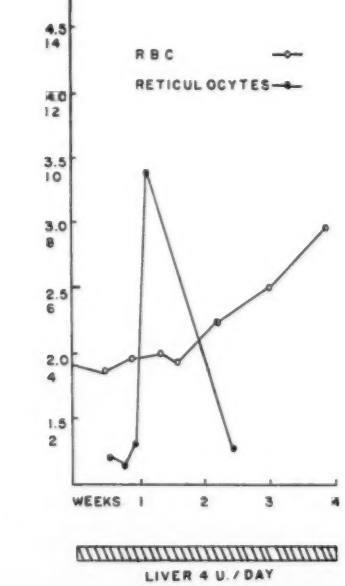
He was admitted on July 18, 1950 for the sixth time. He was very weak, and appeared to be critically ill. The hemoglobin at that time was 4.5 grams per 100 ml., the erythrocyte count was 1.37 x 10^6, the leukocyte count was 103,000 with 3 per cent progranulocytes, 40 per cent myelocytes, 32 per cent metamyelocytes, 17 per cent bands, 3 per cent segmented neutrophils, 4 per cent lymphocytes, and 1 per cent monocytes. He was given 2,000 cc. of whole blood but failed to respond. On the sixth hospital day just prior to his death, the white blood count was 275,000 with 87 per cent myelocytes, 10 per cent metamyelocytes, and 3 per cent bands.

The significant findings at autopsy were leukemic infiltrations of myocardium, lungs, liver, spleen, gallbladder, kidneys, adrenals, lymph nodes, and skin. The gastric mucosa was atrophic.

DISCUSSION

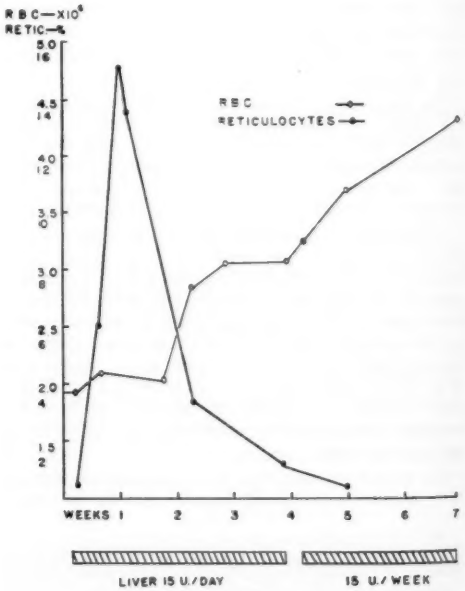
The diagnosis of pernicious anemia in this patient was well established by peripheral blood studies, bone marrow examinations, absence of free hydrochloric acid in the stomach, and an adequate reticulocyte and erythrocyte response to liver, folic acid, and vitamin B_{12}. Neurological findings consistent with pernicious anemia improved with therapy. The patient subsequently developed acute granulocytic leukemia which was well substantiated by the clinical course, peripheral blood studies, bone marrow examinations, and autopsy findings.

Case reports are available on four patients in whom pernicious anemia and granulocytic leukemia coexisted.[1-4] In three of four cases[2-4] the course of the disease was very similar to the sequence of events in the patient reported here, in that the pernicious anemia preceded the leukemia by several years, and the leukemia was rapidly fatal. The coexistence of pernicious anemia and chronic lymphocytic leukemia also has been noted.[5,6] A distinction should be made between the coexistence of pernicious anemia and leukemia and the condition described by von Leube[7] in 1900 under the term leukanemia. This condition in which the blood picture resembles both pernicious anemia and leukemia occurs in the later phases of true granulocytic leukemia. It is not a clinical entity and the term has only descriptive value. Foy and associates[8] reviewed the literature on leukanemia in 1946. They considered only nine of the 31 cases reported in the literature to be acceptable.



SECOND ADMISSION

Fig. 2



THIRD ADMISSION

Fig. 3

The leuko-erythroblastic reaction of bone marrow to the presence of foreign cells may resemble leukanemia.

Although the anemia associated with leukanemia is usually normocytic normochromic, it may be macrocytic. A macrocytic anemia, leukopenia, and thrombocytopenia occurring during the course of a leukemia causes difficulty in differential diagnosis which can usually be resolved by examination of the bone marrow or the finding of leukemic cells in the peripheral blood. Erythrocytes of any stage of development often occur in the peripheral blood in leukemia. Some patients with pernicious anemia in relapse will have myelocytes and even myeloblasts in the peripheral blood. During remission a left shift in granulopoiesis may occur. Adequate response to therapy, bone marrow examination and autopsy findings are necessary to establish clearly the diagnosis of both diseases in the same patient.

Is the occurrence of both pernicious anemia and leukemia in the same patient merely coincidence, or does it indicate a fundamental defect in hematopoiesis common to both diseases? The rarity of this association lends support to the former view. In the five reported cases, including our own, leukemia occurred terminally after several years of continuous or interrupted treatment of pernicious anemia. In animals[9] [10] and man, potent liver preparations affect granulopoiesis as well as erythropoiesis. The granulocytopenia which developed on diets deficient in pteroylglutamic acid led to the use of pteroylglutamic antagonists in the treatment of leukemia. The possible role of the liver extracts, pteroylglutamic acid, and vitamin B_{12} in stimulating abnormal granulopoiesis deserves investigation.

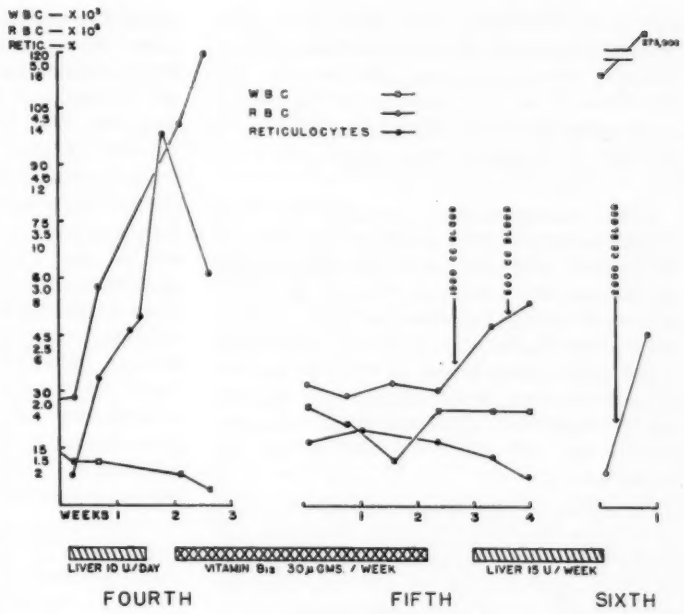


FIG. 4

SUMMARY

(1) A case of a patient with pernicious anemia developing acute granulocytic leukemia is reported.

(2) The coexistence of the two diseases is rare and is probably a coincidence.

(3) The possible role of liver extracts, pteroylglutamic acid, and vitamin B_{12} in stimulating abnormal granulopoiesis deserves investigation.

BIBLIOGRAPHY

1. Sinek, F.; and Kohn, E.: Coexistance of Pernicious Anemia and Chronic Myelogenous Leukemia. Folia Hematol., **42**:180 (Oct.) 1930.
2. Sterne, E. H.; Schiro, H.; and Molle, W.: Pernicious Anemia Complicated by Myelogenous Leukemia. Amer. J. Med. Sci., **202**:167 (Aug.) 1941.
3. Woolley, P. B.: Myelogenous Leukemia Complicating Pernicious Anemia. Lancet, **1**:85 (Jan. 15) 1944.
4. Townsend, S. R.: Pernicious Anemia Complicated by Myelogenous Leukemia. Canad. Med. Assn. J., **61**:417 (Oct.) 1949.
5. Rich, M. L.; and Schiff, L.: A Case of Pernicious Anemia and Chronic Lymphatic Leukemia. Ann. Int. Med., **10**:252 (Aug.) 1936.
6. Mason, J.; and Schwartz, S. O.: The Coexistence of Pernicious Anemia and Chronic Lymphatic Leukemia. Ill. Med. J., **96**:197 (Sept.) 1949.
7. Von Leube, W.: Uber einen Fall von rapid verlaufender schwerer An amie mit gleuchzeitiger leukamischer Beschoffenheit des Blutes. Sitzungsb. d. phys. med. Geseusch. zu Wurgb., Nos. 3 & 4, 46-54, 1900.
8. Foy, H.; Kondi, A.; and Murry, J. F.: The Syndrome of Leukanemia; Report of a Case. J. Path. and Bact., **58**:157 (Apr.) 1946.
9. Langston, W. C.; Darby, W. J.; Shukers, C. F.; and Day, P. L.: Nutritional Cytopenia (Vitamin M Deficiency) in the Monkey. J. Exper. Med., **68**:932 (Dec.) 1938.
10. Pfiffner, J. J.; and Hogan, A. G.: The Newer Hematopoietic Factors of the Vitamin B-Complex. Vitamins and Hormones, vol. 4, pp. 1-34. New York: Academic Press Inc., 1946.

TREATMENT OF ACUTE HEMATOGENOUS OSTEOMYELITIS IN CHILDREN*

By BLAIR E. BATSON, M.D.
Nashville, Tennessee

Acute hematogenous osteomyelitis was long dreaded because of its considerable mortality and the frequent occurrence of chronic infection and deformity in the survivors. Prior to the introduction of modern antibacterial and antitoxin therapy, the death rate in acutely ill patients (those with a temperature of 103° F. or with a heavily positive blood culture) was approximately 46 per cent, while that in the remaining patients was 3 per cent.[1] The over-all rate was 26 per cent.

The number of deaths was reduced effectively for the first time by Dolman[2] in 1934. He and Baker[3] each added staphylococcus antitoxin to the then current surgical therapy. The resulting mortality rate in the total of 67 patients, all of whom had septicemia, was 28.5 per cent.

At the same time, a few surgeons[4 5 6] began to challenge the firmly entrenched dictum of emergency, and often radical, bone surgery.[7] They decreased their mortality significantly by delaying bone decompression for several days. Others,[8 9] who agreed with this mode of treatment, emphasized the immediate and continued need for repair of fluid and electrolyte imbalance, blood transfusions, sedation and immobilization of the affected part.

In 1941, Bagley,[9] using a bacteriophage, reported only one death in 13 patients with uncomplicated staphylococcal septicemia. Obscuring this therapeutic advance were the universally good reports on the use of sulfathiazole and sulfadiazine in staphylococcal infections. The mortality rate in all cases of acute hematogenous osteomyelitis had been cut to an amazing 5 per cent.

Attention was then directed to the prevention of chronic infection. Before the sulfonamides were used, Kenney[1] reported that, of the survivors, 33 per cent had metastases, 33 per cent required sequestrectomy, one-third had a resultant deformity and only 50 per cent eventually healed (criteria not stated). The addition of the sulfonamides to delayed surgery and good supportive care resulted only in a reduction in metastatic lesions.[10–14]

Nachlas[15] said that a few physicians had come to feel that surgery might lead to more harm than good by: (1) converting a closed infection into an open draining wound, a fertile, easily available site for secondary invaders; (2) facilitating implantation of the organism during the bacteremic phase; (3) decreasing blood flow to the area. Robertson,[13] Baker[14] and Hoyt, *et alii*[14] limited their treatment to aspiration of abscesses, sulfonamides and supportive measures. This plan of care resulted in the first noteworthy decrease in the amount of sequestration and chronic osteomyelitis.

MATERIAL AND METHOD

It is the purpose of this report to present the results of treatment of all childhood cases of acute hematogenous osteomyelitis of the long bones that have been seen at Vanderbilt University Hospital since penicillin has been available. All 33 patients were less than 15 years old. No patient was included whose symptoms had been present for more than 30 days; actually, the great majority had had symptoms for less than 10 days. The patients were divided into two groups: Group A contains 21 patients who had definite bone changes on x-ray; Group B contains 12 patients who showed classical signs and symptoms of acute osteomyelitis: fever, pain, localized tenderness and sometimes swelling and redness of the affected area. There were no x-ray changes in this group.

While all patients were treated according to the same general principles, the therapy was not always entirely comparable due to two factors: (1) the limited supply of penicillin available for use in the first patients; (2) indecision in the early days as to the advisability of the use of immediate bone decompression, and of the use of incision and drainage or aspiration of an obvious or suspected abscess. A system of treatment gradually evolved and was used in the majority of patients. Penicillin and sulfadiazine served as the basic chemotherapeutic agents unless the course or laboratory studies suggested

---

*Read in Section on Pediatrics, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

*From the Department of Pediatrics, Vanderbilt University School of Medicine, Nashville, Tennessee.

that the organism was insensitive; then, when available, another therapeutic agent was used. Abscesses and infected joints were aspirated and penicillin or its substitute was instilled into the cavity. Incision and drainage were utilized in the occasional case in which aspiration was unsuccessful. Blood transfusions, reparative fluids and sedation were given as indicated. Immobilization of the affected part was seldom utilized. On discharge from the hospital many of the patients continued to receive small amounts of sulfadiazine for weeks and occasionally months. Weight bearing on involved extremities was forbidden except in those cases with no or minimal changes in the roentgenogram.

Excluded from this study were a number of acutely ill patients who were treated as though they had osteomyelitis. These cases did not show all the classical signs of osteomyelitis but there was little doubt in our minds as to the diagnosis. All of this group who have had follow-up study are clinically well, have had no return of symptoms, and show no changes by x-ray.

RESULTS

Group A (*Table 1*).—The 21 patients included here all had x-ray changes of osteomyelitis. For the purpose of evaluation this group has been subdivided. The first three groups (1-A, 2-A, 3-A) have been adequately followed and are separated according to the roentgenographic picture at present. The other two groups (4-A, 5-A) consist of the patients treated recently and those who have not had adequate follow-up x-rays.

Group 1-A.—The 10 patients included here now have normal bone architecture. There is minimal residual cortical thickening in three of this group. One child shows a metaphyseal deformity which does not impair function. Seven of this group had sterile blood cultures; all but one had received penicillin or a sulfonamide prior to admission. One case underwent surgery, a simple skin incision, several days before admission. Fifty per cent of this group had symptoms for five days or less. All but one patient received more than six million units of penicillin; the duration of this treatment varied from two to four weeks. All received sulfonamide therapy. The follow-up period ranged from two to seven and a half years. One sequestrum appeared after cessation of treatment; it was resorbed. A patient who also had septic arthritis now has a normally functioning joint. The significant points in these 10 cases appear to be the presence of penicillin sensitive organisms, the large amount of penicillin given and the relatively short duration of symptoms in half of the patients.

Group 2-A.—These two patients have remained clinically well but still have slight residual bone sclerosis. One blood culture was positive; both had already received sulfonamide treatment. No surgery was done. Symptoms had been present for 11 and 21 days. Cultures of purulent material aspirated from abscesses in both patients grew out a staphylococcus that was insensitive to penicillin; this fact was not discovered until the sixth and eleventh hospital days. Streptomycin, effective *in vitro* against each organism, was then given for 28 and 22 days. Sulfonamides were also given. This group has been followed for three years. A patient who had septic arthritis, now has only 5° limitation of flexion and extension. In this case there was almost complete sequestration of the humerus; resorption was complete. Failure to attain normal bone architecture was thought to be due to the long duration of symptoms and the presence of penicillin-resistant organisms, which led to an even longer delay in providing adequate specific therapy.

Group 3-A.—Three patients now have chronic osteomyelitis. All had positive blood cultures; only one was thought to have received prior chemotherapy. Symptoms had been present for five, six and seven days. One patient was treated with 2.5 million units of penicillin, a sulfonamide and incision and drainage of an abscess. A hemolytic *Staphylococcus aureus,* which was insensitive to one unit of penicillin per cc., was cultured from a draining sinus two weeks after discharge from the hospital. A sequestrectomy was performed three years later. The patient is now working, seven years after onset. Another patient had an osteotomy done on admission. Penicillin, which was started five days after this, totaled only 985,000 units. He also received a sulfonamide. An acute flare-up six years later subsided rapidly with 10 days of penicillin and sulfadiazine therapy. He is clinically well at present, seven and a half years after onset. The

other patient was treated with osteotomy, a sulfonamide and penicillin; the latter amounted to only 550,000 units over a 22-day period. Several metastatic foci appeared. After arthrostomy of each hip joint, secondary infection with gram-negative bacteria developed. This child is now invalided nine years later with severe deformities of both hips. These failures were due to either penicillin-resistant organisms, grossly inadequate penicillin therapy or secondary infection.

Group 4-A.—The two patients in this group

Case	Surgery	Duration of Symptoms	Total Penicillin in Millions	Duration Penicillin Therapy	Penicillin-Resistant Organisms	Therapy of Resistant Organisms	Sulfa Rx	Follow-up Period	Result by X-ray Remarks
GROUP 1-A									
O. A.	None	9 days	11.14	29 days	—	—	Yes	3 yrs.	Normal bone architecture
J. A.	Skin incision	15 days	1.5	15 days	—	—	Yes	7 9/12 yrs.	Normal bone architecture
T. B.	None	9 days	16.9	28 days	—	—	Yes	2 2/12 yrs.	Normal bone architecture
P. D.	None	5 days	14.9	29 days	—	—	Yes	4 3/12 yrs.	Normal bone architecture
V. H.	None	1 day	10.8	30 days	—	—	Yes	3 8/12 yrs.	Normal bone architecture
C. H.	None	3 days	9.6	14 days	—	—	Yes	3 10/12 yrs.	Normal bone architecture
D. H.	None	21 days	9.5	21 days	—	—	Yes	3 2/12 yrs.	Normal bone architecture
D. Mc.	None	3 days	7.4	27 days	—	—	Yes	4 yrs.	Normal bone architecture
K. R.	None	1 day	6.4	14 days	—	—	Yes	2 4/12 yrs.	Normal bone architecture
N. W.	None	8 days	6.7	17 days	—	—	Yes	3 4/12 yrs.	Normal bone architecture
GROUP 2-A									
F. S.	None	11 days	27.7	34 days	Yes	Streptomycin 28 days	Yes	2 11/12 yrs.	Slight bony sclerosis
M. T.	None	21 days	7.8	11 days	Yes	Streptomycin 22 days	Yes	3 1/12 yrs.	Slight bony sclerosis
GROUP 3-A									
H. B.	I and D abscess	7 days	2.5	20 days	Yes	Not Available	Yes	3 yrs. 7 yrs.	Sequestrectomy Chronic osteomyelitis
B. C.	Osteotomy	5 days	0.985	14 days	None	—	Yes	7 6/12 yrs.	Chronic osteomyelitis
D. S.	Osteotomy Arthrostomy	6 days	0.55	22 days	Secondary infection	Not Available	Yes	5 3/12 yrs. 9 yrs.	Chronic osteomyelitis Crippling deformities
GROUP 4-A									
P. K.	None	7 days	—	—	Probable	Terramycin 27 days	No	6 mos.	Almost complete regeneration
J. H.	None	1 day	11.1	14 days	—	—	Yes	11 mos.	Slight bony sclerosis
GROUP 5-A									
B. A.	I and D abscess	4 days	21.1	34 days	—	—	Yes	5 mos. 4 yrs.	No improvement Clinically well
C. F.	None	6 days	1.85	5 days	—	—	Yes	3 10/12 yrs.	Clinically well
B. M.	I and D abscess	11 days	0.235	11 days	—	—	Yes	2 yrs. 9 3/12 yrs.	Bony sclerosis Clinically well
B. H.	None	9 days	1.9	18 days	—	—	No	2 mos.	Regeneration noted

TABLE 1

had their disease only six and eleven months ago and it is too soon to pass final judgment in this group. No surgery was done. A patient, who had a positive blood culture, was treated with terramycin because of no response after two days penicillin therapy elsewhere. The other case received penicillin and a sulfonamide. Both are clinically well; the first shows almost complete restoration of bone architecture while the other still shows a few areas of sclerosis and translucency.

Group 5-A.—The four patients comprising this group have not had adequate post-treatment roentgenograms. Two of them had received prior chemotherapy; their blood cultures were negative. Of these two, a patient who received adequate penicillin and sulfonamide therapy required incision and drainage of an abscess on the fifteenth hospital day. Five months after onset an x-ray showed sclerosis, rarefaction and a small sequestrum. She has remained clinically well for the intervening four years. The other patient received adequate chemotherapy. An x-ray six weeks later revealed filling-in of the area of destruction. She has had no difficulties in the three and a half years since this. The remaining two patients had positive blood cultures. One of these received only 235,000 units of penicillin. Three abscesses were incised and drained. Bone sclerosis was present two years later. She has remained asymptomatic for the nine years since onset. The other patient, who received 1.9 million units of penicillin, could not be located. On her last visit, two months after onset, an x-ray showed improvement.

Group B (*Table 2*).—This group consists of 12 patients with the typical clinical picture of osteomyelitis but in whom no x-ray changes were ever demonstrated. One patient died; he will be discussed separately from the group as a whole. Only three cases had x-ray frequently enough to be sure that no visible bone change was ever present. Five others had single follow-up x-rays done from five months to four years after onset. The three remaining patients, clinically well several years after treatment, had no x-rays after the third week of their disease. In view of our experience, it is possible that the latter eight cases might have shown changes with properly timed follow-up x-rays. Blood cultures were positive in two instances; in four others prior treatment with penicillin or a sulfonamide had been given. No surgery was done. The duration of symptoms ranged from one to seven days, the average being 3.1 days. Total penicillin given ranged from 1.5 to 10.6 million units, the average being 6.1 million units; this therapy was given over a two to four week period. Nine patients received sulfonamides.

Case	Surgery	Duration of Symptoms	Total Penicillin in Millions	Duration Penicillin Therapy	Penicillin-Resistant Organisms	Therapy of Resistant Organisms	Sulfa Rx	Follow-up Period	Result by X-ray Remarks
GROUP B									
J. K.	None	2 days	10.6	28 days	—	—	No	8 wks. 3 3/12 yrs.	No bone changes
J. N.	None	3 days	10.1	14 days	—	—	Yes	7 wks. 2 yrs.	No bone changes
S. S.	None	2 days	9.8	15 days	—	—	Yes	6 wks. 5 mos.	No bone changes
D. B.	None	2 days	4.3	19 days	—	—	Yes	3 9/12 yrs.	No bone changes
R. C.	None	2 days	2.1	17 days	—	—	Yes	5 mos. 6 4/12 yrs.	No bone changes
B. W. M.	None	5 days	9.8	23 days	—	—	Yes	4 yrs.	No bone changes
N. M.	None	7 days	4.9	15 days	—	—	Yes	1 2/12 yrs.	No bone changes
O. M.	None	3 days	5.5	21 days	—	—	Yes	2 yrs.	No bone changes
C. S. H.	None	1 day	1.5	14 days	—	—	Yes	6 5/12 yrs.	No bone changes
M. H.	None	4 days	2.4	17 days	—	—	No	6 3/12 yrs.	Clinically well
R. P.	None	3 days	5.5	17 days	—	—	Yes	3 1/12 yrs.	Clinically well
R. A.	None	4 days	0.11	16½ hrs.	?	—	No	—	Died

TABLE 2

The excellent results in this group are attributed to early diagnosis, adequate penicillin treatment and the presence of penicillin-sensitive organisms.

There is another patient who falls into this group. He had had symptoms referable to his leg for four days. He was admitted to the hospital in a critical condition. Secondarily infected lesions of chickenpox, signs of osteomyelitis, delirium and a temperature of 104° F. were present. No x-rays were made. A blood culture grew out 1,015 colonies of hemolytic *Staphylococcus aureus* per cc. the next day. He steadily grew worse and expired sixteen and a half hours after admission. He had received supportive therapy and only 110,000 units of penicillin. The organism was not tested for sensitivity. Death was due to overwhelming septicemia.

Our mortality rate was 3 per cent. Others have reported rates of 1 to 3 per cent with the use of penicillin therapy.

DISCUSSION

Acute hematogenous osteomyelitis is a disease in which the initial phase is a bacteremia; in nearly 80 per cent of the cases the primary focus appears to be a skin infection. The organism, usually a hemolytic *Staphylococcus aureus*, settles most frequently in the metaphysis of a growing bone, although any portion may be involved initially. Trauma probably plays a considerable part in determining whether bone infection occurs during any bacteremia. Once the infection is established, pus continues to form until it is under considerable tension. The necrosis resulting from pressure and the action of the staphylococcal toxins leads to rupture into the medullary cavity, subperiosteally or across the epiphysis. Later rupture through the periosteum frequently occurs.

We feel that in those patients who continued to have normal roentgenograms, sufficient necrosis to give rise to demonstrable changes did not occur because the infection was eradicated by rapid and adequate treatment. We should like to emphasize that it is most unlikely that many of the patients in this group would have escaped osteotomy prior to the beginning of this study. Exactly similar cases[15–19] have been reported elsewhere.

The results of this report indicate that restoration of normal bone architecture can be achieved in the majority of cases by adequate medical therapy alone. Caldwell[19] and Altemeier[20] both have reported large series of similarly treated cases with adequate follow-up study. Their results parallel those reported here. Early recognition of the disease and immediate institution of vigorous therapy is of the utmost importance. If other tenets of treatment to be outlined are followed, results will improve chiefly by earlier diagnosis and treatment. We believe that death and crippling due to acute hematogenous osteomyelitis would almost become a rarity if such therapy could be started in the first 24 to 48 hours.

If early treatment is of such great import, then who is to be treated? Of course the patient with a classical picture of the disease must be. Ewing's tumor of bone may simulate this picture exactly. If the patient is seen in the first days of symptoms, the x-ray will show no changes if acute osteomyelitis is present. The thromboses of small or large blood vessels of the bone that occasionally occur in sickle cell anemia may give rise to an absolutely similar group of signs and symptoms and rarely to roentgenographic evidence of bone necrosis. Active sickling of red blood cells aids in the differential diagnosis. However, pyogenic osteomyelitis in patients with active sickling has been reported by Diggs.[21] Most of our own troubles have centered around the possibility of early rheumatic fever in the atypical case. Scurvy, syphilis, osteogenic sarcoma and leukemia may mimic some of the characteristics of the disease. X-rays and the history usually afford an immediate accurate diagnosis in this latter group; serologic tests and peripheral blood or bone marrow studies may be necessary in some instances to rule out acute pyogenic infection. Cellulitis and thrombophlebitis may present a problem in differential diagnosis. Septic arthritis is no problem as these patients are treated by the same regime. Our experience has shown that some patients do not have the classical picture of the disease; thus if one is in doubt, he should not procrastinate, but treat the patient for osteomyelitis. There is no evidence that penicillin or any of the other effective drugs have a deleterious effect on any of the afore-mentioned diseases. Once therapy is begun, it should be continued in its entirety unless another diagnosis is

established beyond all doubt. The importance of early treatment is unanimously endorsed in all previous reports.

Correction of fluid and electrolyte imbalance and the judicial use of blood transfusions have been life-saving in some of our patients. Immobilization was rarely used. We feel that its only use is in the patient who is in danger of a pathological fracture.

Penicillin in dosages of 50 to 100,000 units every three hours and full doses of sulfadiazine until the temperature is normal appear to be indicated. Treatment should be continued with the same or only moderately reduced dosage until at least two weeks have elapsed and until the temperature has been normal at least one week. Sulfadiazine in full dosage has usually been continued for a minimum of four to six weeks in these patients; it is impossible to evaluate the part it has played. A comparison of previous reports leaves no doubt that the best results have been achieved with the larger doses of penicillin.

Daily aspiration of fluctuant abscesses and infected joints, followed by instillation of 50 to 100,000 units into the cavity, has apparently speeded recovery without leading to secondary infection. Many authors advocate this treatment while others feel strongly that abscesses should be incised, drained and closed by primary suture; the latter maneuver is done to prevent secondary infection. Trueta[22] has treated 60 cases with penicillin over a three and a half year period. If pus and dead bone were thought to be present, the affected bone was drilled 12-24 hours later at several places until pus was no longer obtained. After all pus was removed, the wound was closed by primary suture. Full function, sound healing and minimal bone scarring were the results in 52 cases. Considerable bone scarring occurred in four patients. Two have had flare-ups, one has a draining sinus and one considerable joint deformity.

Failure of early recognition of the possibility of penicillin-resistant strains of staphylococcus led to very delayed therapy in two patients. If an organism can be grown from the blood stream or pus obtained by aspiration, sensitivity tests to the various effective agents should be performed and treatment modified if indicated. If sensitivity tests are not available, failure of the patient to show a definite response in 48-72 hours is an indication to change drugs. Spink[23] has grown organisms from a great many patients with staphylococcal disease. He showed that the percentage of penicillin-resistant stains had risen from 12 per cent in 1942 to 50 per cent in 1949-50. Sherris and Florey[24] had similar results but said that most of the staphylococci isolated from acute osteomyelitis were penicillin sensitive. Spink[23] found, that of all the drugs now available, aureomycin was most effective against his strains of penicillin-resistant staphylococci. Thus it may be that aureomycin is the drug of choice. The use of penicillin and aureomycin in combination must be viewed with caution until further results are available. Lankford and Lacy[25] reported diminished antistaphylococcic activity *in vitro* with such a combination.

The appearance of sequestra in an adequately treated patient who has no symptoms is not an indication for operation. Dead, noninfected bone acts as a sterile bone graft does; this was well demonstrated by Cressman and Blalock[26] in 1939. Many authors have also reported the disappearance of sequestra in patients[19 27-33] treated much as ours were.

Weight bearing should be prohibited when there is a considerable area of destruction in a lower extremity. If chronic osteomyelitis does result, Regen[34] has shown that exacerbations may be sharply decreased by the use of small daily doses of sulfadiazine. Recurrences should be treated just as an acute case would be, but with special emphasis on obtaining the causative organism for sensitivity studies.

TREATMENT PLAN

From our experience we suggest that the following outline of therapy be followed in all cases of acute hematogenous osteomyelitis.

(1) *Antibiotics.*—Penicillin, 50-100,000 units every three hours. Full doses of sulfadiazine. Aureomycin, streptomycin, terramycin or chloramphenicol to be substituted if no improvement is noted in 48-72 hours or if sensitivity studies of the causative organism so indicate.

(2) *Duration of Antibiotic Treatment.*—A minimum of two weeks and until the temperature has been normal for at least one week.

(3) *Supportive Care.*—Maintenance of fluid and electrolyte balance, sedation as indicated, and occasionally blood transfusions.

(4) *Abscesses and Injected Joints.*—Aspiration daily followed by instillation of 50-100,000 units of penicillin or its substitute. Incision, drainage and closure by primary suture to be done if aspiration is unsuccessful.

CONCLUSIONS

The early use of large amounts of effective antibiotic drugs, aspiration of abscesses and septic joints followed by instillation of antibiotic drugs and general supportive measures have resulted in a low mortality, high cure rate and a low incidence of residual change and infection in 33 cases of acute hematogenous osteomyelitis in childhood.

REFERENCES

1. Kenney, W. E.: Prognosis in Acute Hematogenous Osteomyelitis with and without Chemotherapy. Surg., **16**:477-484, 1944.
2. Dolman, C. E.: Staphylococcus Antitoxic Serum in Treatment of Acute Staphylococcal Infections and Toxaemias. Canad. M. A. J., **31**:1-8 (July), 130-135 (Aug.), 1934.
3. Baker, L. D.; and Shands, A. R.: Acute Osteomyelitis with Staphylococcemia; Clinical Report on Use of Antitoxin in Its Treatment. J.A.M.A., **113**:2119-2124, 1939.
4. Pyrah, L. N.; and Pain, A. B.: Acute Infective Osteomyelitis; Review of 262 Cases. Brit. J. Surg., **20**:590-601, 1933.
5. Crossan, E. T.: Conservative Treatment of Acute Hematogenous Osteomyelitis. Ann. Surg., **103**:605-612, 1936.
6. Brown, H. P., Jr.: Acute Hematogenous Osteomyelitis of Long Bones; Clinical Review of 160 Cases. Ann. Surg., **109**: 596-614, 1939.
7. Cutting, R. A.: Acute Hematogenous Osteomyelitis of Adolescence. Internat. Abstract Surg., pp. 5-12 (July) 1930.
8. Mahorner, H.; and Crain, A. P., Jr.: Acute Hematogenous Osteomyelitis. Ann. Surg., **115**:790-815, 1942.
9. Bagley, C. E.: Discussion of The Clinical Diagnosis, Prognosis and Treatment of Acute Hematogenous Osteomyelitis, by F. D. Dickson. J.A.M.A., **127**:212-219, 1945.
10. Penberthy, G. C.; and Weller, C. N.: Chemotherapy As Aid in Management of Acute Osteomyelitis. Ann. Surg., **114**:129-146, 1941.
11. Wilson, J. C.; and McKeever, F. M.: Role of Sulfonamide Drugs in Hematogenous (Staphylococcic, Osteomyelitis). J. Bone and Joint Surg., **25**:41-48, 1943.
12. L'Episcopo, J. B.; and Hagerty, E. D.: Conservative Management of Acute Osteomyelitis. N. Y. State J. Med., **43**:853-856, 1943.
13. Robertson, D. E.: Medical Treatment of Hematogenous Osteomyelitis (with Sulfathiazole and Sulfadiazine, Sulfonamides). Ann. Surg., **118**:318-328, 1943.
14. Hoyte, W. A.: Discussion of Open Versus Closed Treatment Osteomyelitis, by L. D. Baker, *et alii*. J. Bone and Joint Surg., **26**:345-349, 1944.
15. Nachlas, I. W.; and Markheim, H. R.: Acute Hematogenous Osteomyelitis; A Study of Treatment. J. Bone and Joint Surg., **30A**:673-679, 1948.
16. Agerholm, M.; and Trueta, J.: Acute Hematogenous Osteomyelitis Treated with Penicillin. Lancet, **1**:877-881, 1946.
17. Higgins, T. T.; Browne, D.; and Bodian, M.: A Penicillin-Treated Series of Cases of Osteomyelitis in Childhood. Brit. M. J., **1**:757-761, 1947.
18. Self, E. B.: Acute Hematogenous Osteomyelitis. Pediatrics, **1**:617-628, 1948.
19. Caldwell, G. A.; and Wickstrom, J.: The Closed Treatment of Acute Hematogenous Osteomyelitis. Results in 67 Cases. Ann. Surg., **131**:734-742, 1950.
20. Altemeier, W. A.; and Walsworth, C. L.: An Evaluation of Penicillin Therapy in Acute Hematogenous Osteomyelitis. J. Bone and Joint Surg., **30A**:657-673, 1948.
21. Diggs, L. W.; Pulliam, H. N.; and King, J. C.: Bone Changes in Sickle Cell Anemia. Sou. Med. J., **30**:249-259, 1937.
22. Trueta, J.; and Agerholm, M.: Acute Hematogenous Osteomyelitis. Diagnosis and Treatment. Post Grad. M. J., **24**: 229-240, 1948.
23. Spink, W. W.: Clinical and Biologic Significance of Penicillin-Resistant Staphylococci, Including Observations with Streptomycin, Aureomycin, Chloramphenicol and Terramycin. J. Lab. and Clin. Med., **37**:278-293, 1951.
24. Sherris, J. C.; and Florey, M. E.: Relation of Penicillin Sensitivity in Staphylococci to Clinical Manifestations of Infection. Lancet, **1**:309-312, 1951.
25. Lankford, C. E.; and Lacy, H.: In Vitro Response of Staphylococcus to Aureomycin, Streptomycin, and Penicillin. Texas Rep. Biol. and Med., **7**:111-124, 1949.
26. Cressman, R. D.; and Blalock, A.: Experimental Osteomyelitis: Effects on Ribs of Increased Intramedullary Pressure and of Toxin- and Nontoxin-Producing Strains of Staphylococci. Surg., **6**:535-549, 1939.
27. Altemeier, W. A.; and Reinecke, H. G.: Roentgenographic Interpretation of Acute Hematogenous Osteomyelitis Treated with Penicillin. Am. J. Roentgenol., **54**:437-448, 1945.
28. Hamilton, J. F.; and Boyd, H. B.: Penicillin in the Treatment of Acute Osteomyelitis; with Case Reports. Sou. Med. J., **39**:597-608, 1946.
29. Killefer, J. J.; and Robertson, R. C.: Non-Operative Treatment of Acute Hematogenous Osteomyelitis: Preliminary Report. J. Tennessee M. A., **40**:319-325, 1947.
30. Dennison, W. M.: Hematogenous Osteitis in Children; Preliminary Report on Treatment with Penicillin. J. Bone and Joint Surg., **30B**:110-123, 1948.
31. O'Brien, R. M.; and Mira, J. J.: Acute Hematogenous Osteomyelitis; an End Result Study of Non-Surgical Treatment with Penicillin and Sulfonamides. J. Missouri M. A., **45**:754-758, 1948.
32. Wilkinson, F. R.: Early Treatment of Acute Hematogenous Osteomyelitis in Children. Pediat., **1**:796-798, 1948.
33. Beerman, C. A.: Acute Hematogenous Osteomyelitis of Long Bones in Infants and Children. J. Pediat., **33**:578-590, 1948.
34. Regen, E.: Unpublished data.

DISCUSSION (*Abstract*)

Dr. B. F. Boylston, Houston, Tex.—It is a pleasure for me, an orthopedic surgeon, to have the opportunity to discuss this paper.

A word of caution is in order about making a diagnosis of acute osteomyelitis in the absence of a bacteriological diagnosis and x-ray changes. This is particularly true in a statistical study such as the author has presented. In making a specific diagnosis of acute osteomyelitis one must remember that in septicemia, bone and joint pains are common. In the group A cases there were 12 cases with three positive blood cultures. In other words, a bacteriological diagnosis was not made in nine of these cases and they failed to show x-ray changes at any time.

The common recent mistakes in early diagnosis that I have seen are: (1) a diagnosis of deep cellulitis for an acute osteomyelitis of the lower end of the femur; (2) a diagnosis of a septic knee joint in the absence of excess fluid; (3) a diagnosis of fever of undetermined origin in an infant in the presence of a septic hip that was picked up by an intravenous pyelogram.

The x-ray changes associated with scurvy, syphilis and tumor that one may confuse with acute osteomyelitis do not develop in the latter for two to three weeks after the onset. We are all in agreement that it is much better to treat a case of acute rheumatic fever a few days than it is to delay in treating acute osteomyelitis.

I am against early operative treatment in acute osteomyelitis of the long bones as previously practiced within 48 to 72 hours after onset; not because of the danger of spread of infection or interference with blood supply, but because I do not feel it to be necessary. The immediate problem is the control of septicemia. Death early in acute osteomyelitis is due to overwhelming infection and subsequently multiple abscesses in the vital organs.

At the Jefferson Davis Hospital on the Orthopedic Service we have been accustomed to using large doses,

for example, 200,000 units of penicillin every three hours even in infants, as approximately 63 per cent of the organisms are hemolytic streptococci in infants and 91 per cent in children are *Staphylococcus aureus* as shown by Green. We find that most organisms are penicillin sensitive. It is interesting that the author found two cases of penicillin-resistant organisms.

The hip joint is an entirely different problem from any other joint or long bone. Destruction of the femoral head is a catastrophe. Early, one cannot differentiate a primary septic hip from an acute osteomyelitis of the femoral neck. It has been our custom to aspirate the hip joint anteriorly and if pus is obtained to instill penicillin into the joint. If after 48 to 72 hours there has been no improvement clinically, then we feel the best chance to save the hip is by open surgical drainage.

Subperiosteal abscess of the long bones we feel should be incised and drained as soon as one can be sure of its presence, the reason being the likelihood of extensive periosteal stripping with subsequent massive sequestration of the shaft. These wounds are closed primarily; the bone is not opened. A catheter is left in the subperiosteal pocket for penicillin irrigations locally. Sequestra, as the author pointed out, need not be removed early as in most instances, particularly if they are large, the chance of revascularization is excellent. To remove a large sequestrum of the shaft of a long bone would mean a complete disruption of its continuity.

It has not been our custom routinely to immobilize the affected extremity by either plaster or traction. However, we are very careful to watch for flexion contractures of the knee and hip, and often use traction in the lower extremity. In the upper extremity the main problem is not so much contracture as it is the prevention of pathological fractures. Here we use bivalve plaster casts.

PATHOLOGY OF ABNORMAL UTERINE BLEEDING*

By RICHARD A. STREET, JR., M.D.
Vicksburg, Mississippi

A complete consideration of all aspects of the subject of abnormal uterine bleeding would indeed be long and difficult, since this symptom appears in a large proportion of gynecologic lesions and its significance is generally regarded as proportionately of greater consequence. Briefly, the causes of abnormal uterine bleeding may be classified into three general groups, namely: (1) general causes, such as blood dyscrasias or hypothyroidism; (2) functional causes, with some type of pituitary-ovarian imbalance; and (3) local causes, among which more prominently are mentioned leiomyomata, carcinoma, uterine polyps, retention of products of gestation, adenomyosis, and pelvic inflammatory disease. It is with the last group that I am chiefly concerned in this discussion. While it is admitted that a large number of these patients never need any treatment beyond conservative measures, this study is concerned only with those in whom biopsy, curettage, or removal of affected parts was done. A brief review of the anatomical and physiological factors seems advisable.

In perhaps the most important, and sometimes the gravest group of cases, the bleeding is not in any way related to the menstrual mechanism, being explained by the presence somewhere in the pelvic apparatus of a very tangible lesion of one sort or another. The bleeding, in such cases, may be readily explicable without involving physiological factors, often by such obvious causes as the actual opening of the blood vessels by destructive ulceration. This is pre-eminently the case in the most important variety of all, namely, that associated with malignancy situated in any part of the genital tract.

Bleeding from cervical or endometrial polyps may likewise be easily explained, depending on whether caused by trauma or necrosis.

When the bleeding is caused by leiomyoma the explanation cannot be so stereotyped, as various mechanisms may come into play. The fact that the submucous variety is especially likely to cause bleeding seems explicable by the frequency with which the overlying endometrium undergoes atrophy, infection and ulceration, as well as by the greater impingement upon the endometrial venous channels, from which such bleeding has its source. But bleeding may also be noted with intramural growths, and probably here we must include an effect upon the contractility of the uterine musculature, a factor which many believe is of importance even in the limitation of normal menstrual bleeding. The same factor may be concerned in the menorrhagia which is not infrequently seen with subinvolution of the uterus, especially when associated with marked retrodisplacement, in which case an additional factor may be the venous congestion often associated.

In one of the commonest of all causes of the uterine bleeding, that associated with retention of gestational products after abortion, the mechanism apparently is not always the same. Here again the factor of lessened muscular

*Read in Section on Gynecology, Southern Medical Association, Forty-Fifth Annual Meeting, Dallas, Texas, November 5-8, 1951.

contractility is no doubt sometimes involved, but certainly not always. Free bleeding may be noted from a well contracted uterus many weeks after an early abortion, while in other cases the uterus may be large and boggy, with its cavity full of placental tissue and with no bleeding at all for even weeks. In such cases the bleeding may occur when the uterus finally tries to expell its contents, with opening up of large sinuses, just as the surgeon, in evacuating such retained masses, produces free bleeding when he separates retained masses from the uterine wall. Other possible factors in the bleeding of incomplete abortion are those due to the loss of endometrial surface and the opening of blood vessels, associated inflammation and necrosis. When it comes to the bleeding associated with adnexitis, we cannot always readily offer rational explanations. The endometrium in most cases is histologically normal and yet in at least some cases there may be a shortening of the menstrual interval (polymenorrhea) or an increased menstrual amount (hypermenorrhea). The logical explanation, but one which is not easily demonstrable, is that an ovarian dysfunction is associated with, and possibly engendered by the pelvic pathological process. The same factor may be at play in the polymenorrhea or hypermenorrhea not infrequently associated with leiomyoma. For that matter we cannot exclude consideration of the reciprocal relationship which exists between the ovary and the uterus. One is accustomed to think of the ovaries, through their hormones, as dominating the physiologic lift of the uterus, but there is substantial evidence that the relationship of the two organs is not one-sided, and the uterus, in some still unknown fashion, exerts a reciprocal effect upon the ovaries.

These generalities do not by any means exhaust the genital lesions which may be responsible for uterine bleeding, but they serve to illustrate certain mechanisms, some readily demonstrable and others still theoretical. They emphasize also that even in the presence of definite structural disease, we must in some cases recognize the fact that these exert their bleeding effect through the pathological-physiologic disturbance which they bring about. There are certain other lesions which exhibit this combined anatomic and physiologic etiology much more clearly and understandably, for example: the postmenopausal pseudomenstrual bleeding, characterizing granulosa cell ovarian tumors, ordinarily the result of the estrogen producing function of the tumor. Again the bleeding characteristic of tubal pregnancy is commonly endometrial in origin, due to certain hormonal influences emanating from the tubal trophoblast.

The plan of investigation of each patient who presents herself with a history of abnormal bleeding should be well organized and sufficiently adequate to establish a diagnosis. An accurate statement of the facts about the present irregularity, how long it has existed, and the extent of the loss of blood according to the patient's estimation, is important. Frequently, the statement of excess flow does not fit with the clinical findings. The chief value of the patient's statement is when they agree with the clinical findings and laboratory data.

Besides a thorough general examination, pelvic study should include careful bimanual examination and rectovaginal examination. A careful inspection of the cervix with the speculum is mandatory. Routine laboratory studies including red count, hemoglobin, and a serologic test for lues are certainly essential. Cervical biopsies of every suspicious lesion are routine. Diagnostic curettage is relied upon for a more thorough study of the endometrium, and it is my policy thoroughly to evacuate the contents of the uterus in incompletely expelled products of early gestation when there is evidence of retention of the products, provided no evidence of sepsis is present.

In reviewing 430 cases of abnormal uterine bleeding subjected to surgery or diagnostic procedures involving the obtaining of tissue for examination by the pathologist, Dr. R. H. Fenstermacher, at the Mercy Hospital taken from the files of the Street Clinic during the years 1945, 1946, and 1947, a total of 168 hysterectomies were done, the mean average age of this group being 42.4 years. The most common pathological lesion found was leiomyomata of the uterus, which was diagnosed as the principal disease in 111 of these patients. Adenomyosis of the uterus was the next most frequent lesion in this group being present in 12 cases. Pathologic diagnosis of pelvic inflammatory disease was made in 10 cases. Carcinoma of the uterine fundus was the principal diagnosis

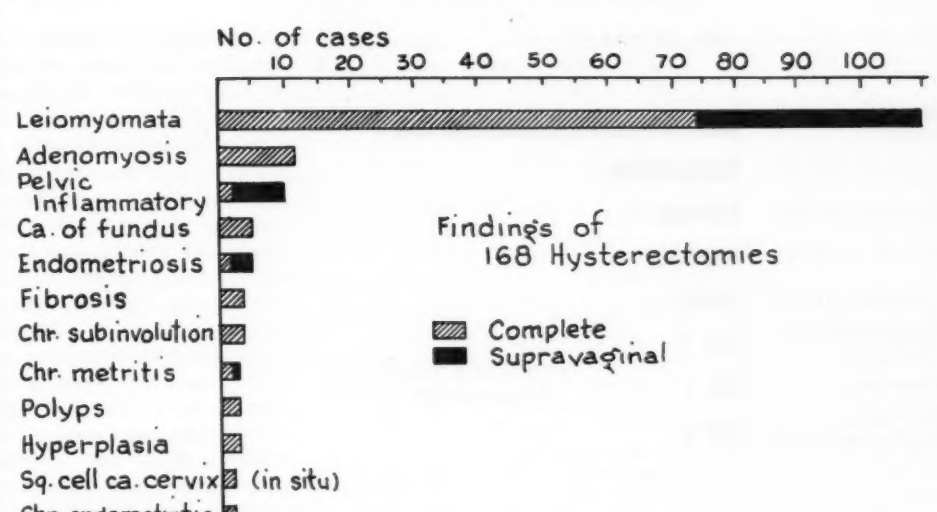


FIG. 1
Hysterectomies.

in five cases. Endometriosis of the ovaries was the primary pathological diagnosis in five cases. Fibrosis uteri and chronic subinvolution of the uterus were the principal diagnoses in four cases each. Hyperplasia of the endometrium, endometrial polyps, and chronic metritis were the primary pathological diagnoses in three cases each, and in each of these three groups the abnormal bleeding occurred either at the menopause or following the menopause. In two cases the primary pathologic diagnosis was squamous cell carcinoma of the cervix (*in situ*). Chronic endometritis was the primary pathological diagnosis in two cases, and myosarcoma of the uterus was the primary diagnosis in two cases.

In the group of dilatation and curettage there were a total of 193 cases. Of this group, 60 tissue studies reported hyperplasia of the endometrium as the primary diagnosis. Curettement for removal of incomplete expulsion of the products of gestation in early pregnancies was also done in 60 cases. In 54 cases the tissue examination gave as the primary diagnosis chronic endometritis. In 12 cases endometrial polyps were the primary diagnosis and in seven cases leiomyomata of the uterus.

In the group of biopsies followed by radium and x-ray therapy, 54 cases of squamous cell carcinoma of the cervix were included. It is interesting to note in this group there were seven

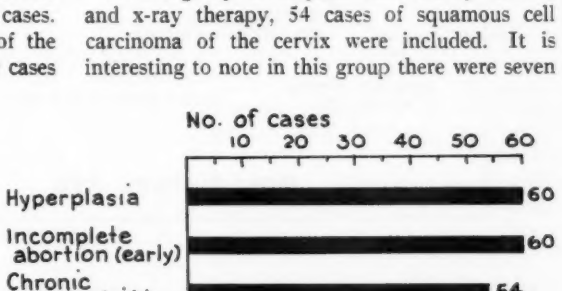


FIG. 2
Dilatation of Curettage.

Biopsy with Radium & X-ray used as follows:

54 cases of sq. cell ca. of cervix. (7 stump ca.)
1 myosarcoma of uterus.
1 ca. of fundus of uterus.

FIG. 3

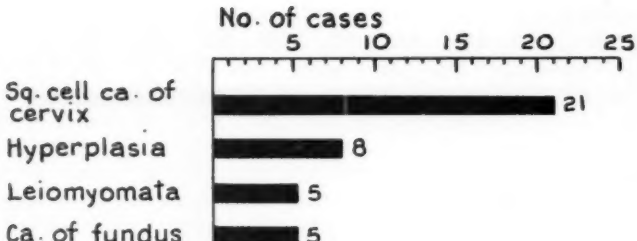


FIG. 4

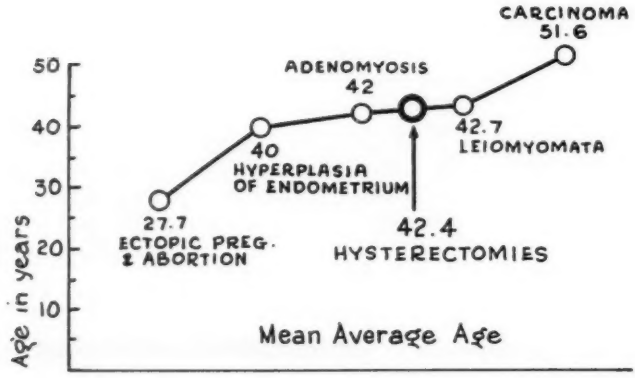


FIG. 5

cases of carcinoma of the cervical stump with a preceding supravaginal hysterectomy. It is also interesting to note that during the same period 10 cases of carcinoma of the cervix had no history of abnormal uterine bleeding. Myosarcoma of the uterus and adenocarcinoma of the uterine fundus were the primary diagnoses in one case each, treated with radium and x-ray.

In the final group of miscellaneous procedures, three cases of pedunculated leiomyoma, which extruded from the cervical canal, were amputated at their base. A case of ovarian endometriosis had a salpingo-oophorectomy of the affected side. Two cases of pelvic inflammatory disease had bilateral salpingo-oophorectomy, and one had right salpingo-oophorectomy with removal of affected parts. Six cases of ectopic pregnancy had salpingo-oophorectomy of the affected side and one case had salpingectomy of the affected side.

In reviewing the number of the various pathological conditions found in postmenopausal bleeding, the commonest lesion which was present was squamous cell carcinoma of the cervix, being the principal diagnosis in 21 cases. Primary diagnosis of hyperplasia of the endometrium was next in frequency, being present in eight cases. Adenocarcinoma of the uterine fundus and leiomyomata of the uterus were both present in five cases, the adenocarcinoma of the fundus being predominantly a postmenopausal group as only six cases of adenocarcinoma of the fundus were reported in the entire series. Adenomyosis was the principal diagnosis in four cases of postmenopausal bleeding. Endometrial polyps was the principal diagnosis in two cases. Fibrosis uteri was the primary diagnosis in two cases, and chronic endometritis was also the primary diagnosis in two cases of the postmenopausal bleeding group.

In summary, the lesions that are associated with abnormal uterine bleeding are many and varied. The analysis of 430 surgically treated cases demonstrates the cause of bleeding only in this group, and thus excludes the large group requiring only medical measures for control. Where multiple lesions were found by the pathologist, the diagnosis most obviously the cause of bleeding was selected.

Review of tissue study of the cases seems to emphasize the danger of the assumption that abnormal uterine bleeding in a woman known to have a definite pathological entity such as leiomyomata, is attributable only to leiomyoma. Such a premise is at times fallacious. We have observed patients only a month or two after a

supracervical hysterectomy, who complained of the same bleeding they had before operation. On examination we have found carcinoma of the cervix which in all probability was present when the fundectomy was done.

We have also done complete hysterectomy for large leiomyomata where the clinical examination of the cervix seemed entirely normal, and yet tissue examination showed the presence of cancer of the cervix in some cases and cancer of endometrial origin in others. Such experience again reminds us that the doctor may take nothing for granted, and in this particular instance if he does he may bring disaster to his patient and all concerned.

BIBLIOGRAPHY

1. Corscaden, James A.: Gynecologic Cancer. New York: Thomas Nelson & Sons, 1951.
2. Counseller, V. S.: Diagnosis and Treatment of Uterine Bleeding in Non-Pregnant Patient. Mississippi Doctor, **26**:31-36 (July) 1948.
3. Frank, I. L.: Uterine Bleeding and Extragenital Disturbances. Amer. J. Med. Sci., **210**:787-798 (Dec.) 1945.
4. Freed, S. C.: Menstrual Dysfunctions: Abnormal Uterine Bleeding. Western J. Surg., **54**:45-49 (Feb.) 1946.
5. Meigs and Sturgis: Progress in Gynecology, Vol. II. New York: Grune & Stratton, 1950.
6. Novak, Emil: Uterine Bleeding with Special Reference to Functional Type. J. Internat. Coll. Surgeons, **11**:9-16 (Jan.-Feb.) 1948.
7. Novak, Emil: A Correlative Study of Adenomyosis and Pelvic Endometriosis, with Special Reference to the Hormonal Reaction of Ectopic Endometrium. Amer. J. Obst. & Gynec., **56**:634-644 (Oct.) 1948.
8. Novak, Emil: Functional Uterine Bleeding. A Summarizing Review. Obst. & Gynec. Surv., **1**:682-698 (Oct.) 1946.
9. Novak, Emil: A Textbook of Gynecology. Third edition. Philadelphia: W. B. Saunders Company, 1948.
10. Pratt, J. P.: Bleeding Associated with Menopause. J.A.M.A., **135**:562-564 (Nov. 1) 1947.

DISCUSSION (*Abstract*)

Dr. John M. Fleming, Spartanburg, S. C.—The medical profession is in disrepute with the public and government because too many patients die with carcinoma of the uterus. Dr. Street stresses the fact that patients may have co-existing fibroid and carcinoma of the uterus.

Most pathologists agree that carcinoma of the cervix begins at the columno-squamous junction and often this area will not be within the visible area of the cervix. Therefore, in doing pelvic examinations, this point must be borne in mind, and adequate means taken to examine this area. The curette, suction and various scraping technics are useful.

Cases of abnormal bleeding should be followed until a definite diagnosis of the cause is established.

Southern Medical Journal

JOURNAL OF THE
SOUTHERN MEDICAL ASSOCIATION

Copyright, Southern Medical Association, 1952. Material in the Southern Medical Journal, being covered by copyright, may not be reproduced in whole or in part or abstracted without permission from the publisher and then only if due credit is given.

Published monthly by the Southern Medical Association, Empire Building, Birmingham 3, Alabama. Annual subscription, $10.00. Single copies 85c each.

Entered as second-class matter at the Post Office at Birmingham, Alabama, under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized December 20, 1921.

Volume 45 JUNE 1952 Number 6

EDITORIAL DEPARTMENT

Editor
M. Y. Dabney, M.D., Birmingham, Alabama

Associate Editors
Curtis J. Lund, M.D., New Orleans, Louisiana
Curtice Rosser, M.D., Dallas, Texas
Tinsley R. Harrison, M.D., Birmingham, Alabama

SOUTHERN MEDICAL ASSOCIATION
Forty-Sixth Annual Meeting
Miami, Florida, November 10-13, 1952

MUMPS DIAGNOSIS

With ingenious new weapons, scientists continue to hack away at the trunk of the virus tree. It has been shown that mumps antibody may be dyed with fluorescein without interfering with its ability to precipitate the virus. In other words: an animal may be immunized to mumps virus; the immune bodies of its serum may be concentrated and combined with fluorescein to make them readily visible; the fluorescein-attached antibody is then incubated with suspected mumps virus in tissue culture or from the parotid gland. Upon microscopic study, if mumps was present in the unknown tissue, the precipitated dyed antigen or mumps virus is visible in characteristic position in the material. If mumps virus is not present, the dyed antibody is not precipitated but washes away from the cells. The result, that is, the presence or absence of mumps virus in the unknown, may be read in a few hours, instead of after waiting for a culture or for animal inoculation.[1]

Cushing and Morgan,[2] at the University of Rochester, have sought vitamin analogues, substances resembling vitamins, which may inhibit viral growth, using mumps and influenza viruses for their study. Many of the currently popular blood stream antiseptics resemble or are vitamin analogues. Their viruses were incubated in chick embyro tissue for twenty-four hours, then the infected nutrient solution was withdrawn and placed with fresh nutrient solution containing the vitamin analogue whose antiviral properties were to be tested. Inhibition of virus growth could be quickly detected if it was achieved. The analogues used were apparently harmless to chick tissue.

Two substances, oxythiamine and desoxypyridoxine, resembling the two B vitamins thiamine and pyridoxine, showed a definite inhibitory effect particularly upon multiplication of mumps virus. Mumps virus was inhibited by exposure to 0.1 mg. per ml. of oxythiamine. Both mumps and influenza viruses were inhibited markedly by exposure to 0.5 mg. per ml. of desoxypyridoxine. These two substances were the most active inhibitors among a group of vitamin analogues tested. It was believed that the analogues exerted their effects upon virus which had had time to enter the host cells.

The infectivity of the virus material and its cell penetration could perhaps be tested by using the dyed antiserum described by Watson,[1] to precipitate virus if present. This technic might speed the search for a virus-inhibiting compound.

CAUSE OF HYPOTENSION AFTER SEVERE BURNS

Within a few days after exposure to atomic explosion, burned subjects may develop a pronounced fall in blood pressure. Its nature and means of prevention have been extensively studied. According to Haley[3] and associates at

1. Watson, Barbara K.: Distribution of Mumps Virus in Tissue Cultures as Determined by Fluorescein-Labeled Antiserum. Proc. Soc. Exper. Biol. and Med., **79**:222 (Feb.) 1952.

2. Cushing, R. T.: and Morgan, H. R.: Effects of Some Metabolic Analogues on Growth of Mumps and Influenza Viruses in Tissue Cultures. Proc. Soc. Exper. Biol. and Med., **79**:497 (Mar.) 1952.

3. Haley, T. J.; Andem, M. R.; Riley, R. F.; and Williams, I.: Identification of Ferritin in Blood of Dogs Subjected to Radiation from an Atomic Detonation. Proc. Soc. Exper. Biol. and Med., **79**:547 (March) 1952.

the University of California Atomic Energy Project, who observed a group of dogs after exposure to an atomic blast, the fall in blood pressure is not due to a direct effect of the burn upon the capillaries, but to the concentration in the blood stream of a vasodepressive agent liberated from the liver. The plasma of the burned dogs contained a toxic material which on injection into normal rats caused a fall in the rats' blood pressure, and a decrease in the epinephrine sensitivity of their capillaries. It was suspected that the vasodepressive agent in the burned dogs' blood was ferritin, an iron-containing protein which is present in the liver of all mammals.

Crystalline ferritin was prepared from normal dog's liver, and an antiserum to it was produced by injection of rabbits. A highly active anti-dog-ferritin serum was obtained. If this antiferritin serum was injected into normal rats, with the vasodepressive plasma of the irradiated dogs or shortly after it, no fall of blood pressure occurred. The vasodepressive agent of the burned dogs' plasma was thus inactivated, a very specific reaction for this protein. Incubation with liver inactivated the vasodepressive dog plasma; incubation with kidney had no effect, and these two reactions likewise characterize ferritin. The vasodepressor did not dialyze. Other reactions were identical with those of ferritin.

This very interesting work raises many questions. Could hypotension of severe human burns be beneficially treated with antiferritin serum? Could any form of clinical hypertension be treated with ferritin itself? What stimulates release of ferratin from the liver?

Long ago McCollum[1] and associates noted that death of laboratory animals in vitamin E deficiency came with a crisis or failure of iron metabolism. Could either shock or hypertension be related to vitamin E disturbances, if deficiency of vitamin E is related to failure of iron assimilation?

Better methods of examining all these problems are constantly being developed and utilized.

1. Simmonds, Nina; Becker, J. E.; and McCollum, E. V.: The Relation of Vitamin E to Iron Assimilation. J.A.M.A. **88**:1047, 1927.

MANGANESE IN DIGESTION

Physiologic studies with radioactive elements (isotopes of the usual known element) are proceeding apace. Though their direct contribution to therapeutics is slight, they provide a new technic of study of tissue function, since their course through the body may be fairly readily followed by estimations of radioactivity. The hypothesis that different elements should regularly localize in specific cells and thus furnish a vehicle to carry a radioactive therapeutic agent to a particular part of the body, has provided a fruitful field for investigation. It must be assumed, of course, that the radioactive element will take the same course in the body as the non-disintegrating one. It should be possible by study of many elements to choose a product which will irradiate almost any specific organ and spare the surrounding tissue.

Manganese is one of the trace minerals in mammalian physiology, yet essential to life and reproduction. In dogs with pancreatic fistula, according to investigators[1] at Oak Ridge, radioactive manganese (Mn^{54}) is shown within twenty minutes after intravenous injection to be concentrated in the liver and pancreas in very much larger quantities than in the blood. The liver level rapidly falls off after an hour, while the pancreas level is sustained for four to five hours. In the case of another isotope of manganese, Mn^{56}, the liver level shows only a slight rise, while the pancreatic level between the second and third hour has a sharp and sustained rise.

In the pancreatic juice of pancreatic fistula dogs, the Mn^{54} level was followed over a period of days. It tended to fluctuate at meal hours, varying with the protein level of the secretion, though it was shown by dialysis studies not to be in protein combination.

The concentration in pancreatic juice, 1.0 to 0.9 per cent of the amount injected after twenty-four hours, was greatly in excess of that in the blood. The chief path of excretion was in the feces. At autopsy after seventy hours, the liver still contained the highest concentration, equal to twice that of the pancreas. The kidneys contained as much as the pancreas, although little is excreted in the urine.

The Oak Ridge investigators suggest that the labeled manganese appears in the pancreas as part of a secretory process. It is present in the pancreatic juice before the element is experi-

1. Burnett, W. T., Jr.; Bigelow, Robert R.; Kimball, Allyn W.; and Sheppard, Charles W.: Radiomanganese Studies on the Mouse, Rat and Pancreatic Fistula Dog. Amer. J. Physiol., **188**:620 (Mar.) 1952.

mentally injected. It varies with the feeding schedule and is proportional to the output of protein nitrogen, which in turn is proportional to the enzyme strength of the juice. Manganese is known to activate many enzyme systems, as well as to have a catalytic action in the preparation of certain inorganic alloys of industry. It is therefore suggested by Burnett and associates that manganese is concerned in the enzyme activity of the pancreatic juice, that is, in the pancreatic digestive function.

TWENTY-FIVE YEARS AGO

From Journals of 1927

Women Doctors in the British Isles.[1]—In the medical journals a surgeon, Mr. William Robinson of Sunderland, calls attention to the glut in women physicians. . . . An excessive number of graduates (men and women) are entering the profession in the face of a fallen and still falling sickness rate. The Medical Register already contains more than 53,000 names. It is said that out of every three qualifying in Ireland, two must emigrate, and the proportion must be higher in Scotland. Mr. Robinson refers, evidently to draw the moral, to the practise of some American universities, which restrict their medical students to a fixed number that can be adequately taught the practical side of their work, some of them admitting less than a fourth of the applicants and selecting only the best after inquiry and examination.

Women Doctors in Austria.[2]—During 1926, the number of women physicians engaged in the practise of medicine in Vienna was augmented . . . 20 per cent. The number of male physicians increased during the same period only 2 per cent. . . . Only twenty years ago it was rather the exception for one of the university instructors to admit women to his lectures . . . a prospective further increase . . . raises the question whether within a definite period male physicians may not become completely superseded. However, it seems probable that men will be more likely to prefer men and women will be more inclined to choose women as their medical advisors.

Crisis in China.[3]—The following record of destructive assaults on various hospitals and medical colleges illustrates the blind fury of the Chinese nationals against the philanthropic institutions which, supported by foreign generosity, have for many years ministered gratuitously to the bodily needs of the local inhabitants and have established educational centers where Chinese students may be trained in the prevention and cure of disease. Dr. Maxwell states that while the Northern troops have been justly accused of looting, he knows of no damage having been done by any retreating [Northern] army, all the outrages being attributable to Southern troops or their civilian sympathizers. From nearly all areas come reports of unprovoked outrages on the foreign and loyal Chinese staffs . . . confiscation and robbery under arms . . . revengeful cruelty to the innocent and unprotected.

Typhoid in Montreal.[4]—The occurrence of thousands of cases of typhoid in Montreal since March is reason for astonishment . . . from January 1 to March 3, 1927, nineteen cases of typhoid occurred in Montreal. This was not regarded as an excessive rate for the city. The present epidemic . . . is said to date from March 4. . . . During the week ended March 21, this number had risen to 497. . . . Montreal newspapers . . . stated that adequate provision was being made for the hospitalization of patients; that persons were being advised to take antityphoid inoculations and that apparently the epidemic was milk-borne. Newspapers said also that some persons thought the epidemic was due to infected water, but that this could not be determined as Montreal had no city bacteriologist! . . . From March 4 to May 20, 3,788 cases of typhoid were reported in Montreal with 291 deaths. . . . The Montreal *Star,* May 19 . . . referred to an order that had been given to close two Montreal dairies but stated that the plants were not yet closed and were still distributing milk. . . . During the early course of the epidemic, the U. S. Department of Agriculture placed an embargo on the shipment of milk from any point in the area included within a radius of two hundred miles from Montreal. . . . The outbreak . . . seems to be definitely limited to Montreal and its immediate vicinity.

Diagnosis of Syphilis.[5]—Since the development of the Wassermann test, almost yearly announcements of precipitation tests for syphilis have ensued. Now that the value and especially the limitations of the Wassermann test have been established, clinicians are turning to precipitation tests and asking whether any of them have superior features. . . . By (1915) it was well established that the Wassermann test was not a specific immunologic reaction and that alcoholic extract of normal heart tissue served well as antigen. . . . During the past few years the Kahn test has aroused much interest. In this test, a cholesterolized alcoholic extract of beef heart is employed as antigen. . . . Any simpler test that is reliable will ultimately replace the more cumbersome Wassermann.

Kahn Test.[6]—Kahn and Wassermann tests were made on 25,741 specimens with relative agreement in 97.8 per cent. The clinical history on 200 specimens in which the Wassermann and Kahn disagreed, indicated that the Kahn test is more sensitive than the Wassermann test in treated cases. The advantages of the Kahn test are in the saving of time, labor, and cost . . . and in reduction of technical error.

1. Foreign Letters. London. J.A.M.A., **88**:1824, 1927.
2. Foreign Letters. Vienna. J.A.M.A., **88**:1825, 1927.
3. Reviews. Brit. Med. J., p. 1013 (June 4) 1927.
4. Editorial: Typhoid Epidemic in Montreal. J.A.M.A., **88**: 1803, 1927.
5. Editorial. Precipitation Tests in the Diagnosis of Syphilis. J.A.M.A., **88**:1714 (May 28) 1927.
6. Hull, Thomas G.: Twenty-Six Thousand Kahn Tests Compared with the Wassermann. J.A.M.A., **88**:1865 (June 11) 1927.

Book Reviews

Aphorisms of Dr. Charles Horace Mayo and Dr. William James Mayo. Collected by Frederick A. Willius, M.D. 109 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1951. Price $2.75.

In collecting these aphorisms from the writings of the famous Mayo brothers, their associate, Dr. Willius, has carefully searched their many papers. This labor of love has been rewarded by a collection which is interesting not only for its contents, but also because it reflects the personalities of the Doctors Mayo. It comes very close to hero worship, however, to apply the term "aphorism" to such truisms as "There are lots of people who think they are sick and who are not sick"; or, "There is a limit to the amount of learning a man can absorb." Portraits of the brothers Mayo, and a speech and letter of Dr. William J. Mayo, round out this beautifully printed and bound volume.

The 1951 Year Book of Drug Therapy (September, 1950-August, 1951). Edited by Harry Beckman, M.D., Director, Departments of Pharmacology, Marquette University Schools of Medicine and Dentistry; Consulting Physician, Milwaukee County General and Columbia Hospitals, Milwaukee, Wisconsin. 502 pages, illustrated. Chicago: Year Book Publishers, Inc., 1951. Price $5.00.

The series of "Year Books" contain summaries of important articles which appeared during the preceding year, with some editorial comment. This volume covers recent advances in drug treatment in medicine, surgery, obstetrics, ophthalmology, pediatrics, and roentgenology. The papers have been selected with care, and in addition to the American literature, a few significant foreign papers have been included. They are arranged according to specialties. This book makes it very convenient to increase one's familiarity with the current literature, and to follow recent trends in drug therapy.

Spatial Vector Electrocardiography: Clinical Electrocardiographic Interpretation. By Robert P. Grant, M.D., National Heart Institute, Bethesda, Maryland; and E. Harvey Estes, Jr., M.D., U. S. Naval Hospital, Bethesda, Maryland. 149 pages with 41 figures. Philadelphia: The Blakiston Company, 1951. Price $4.50.

First published as a manual by Emory University, "Spatial Vector Electrocardiography" by Grant and Estes has now been made available in book form for a wider audience. This new technic in electrocardiographic interpretation is based on rational physical principles rather than empirical observations; since interpretations are derived from standard bipolar and unipolar leads, no special equipment is required. Although traditional methods of electrocardiographic interpretation will probably not be supplanted by the use of vector analysis, greater familiarity with the spatial vector technic will be of value to the electrocardiographer in the interpretation of certain difficult tracings, as well as supplying him with a better comprehension of the physical forces involved. Considering the rather theoretical nature of the subject, the book is very readable; indeed the authors have deliberately avoided references to more complex mathematical considerations for the sake of simplicity. This book is designed more for the advanced student of electrocardiography than for the beginner.

Roentgenologic Diagnosis of Diseases of Bones. By David G. Pugh, Assistant Professor of Radiology, Mayo Foundation, Graduate School, University of Minnesota; Consultant, Section on Roentgenology, the Mayo Clinic, Rochester, Minnesota. 316 pages, illustrated. New York: The Williams & Wilkins Company, 1951. Price $5.00.

The volume is cloth bound, light tan in color and contains the pages represented from Nelson's loose leaf "Diagnostic Roentgenology." The binding, printing and paper are in keeping with the usual high standards of printed material from the Mayo Clinic. By omission of exact references to original articles, the book has become handy in material covered and size of volume. The outline of contents of the book on the initial pages is a complete outline for study of diseases of the bones. Particularly outstanding are the plates showing in diagrammatic fashion the time of appearance of centers of ossification. The illustrative x-ray plates are clear and of good diagnostic quality. The text reflects well and critically the recent changes in the literature, especially those of hyperparathyroidism.

The section on osteochondrosis covers the more common sites of this pathological entity but does not include all sites where this disease may occur. The section on bone tumors is adequate. It would seem desirable, however, to follow the classification of the American College of Surgeons, Bone Tumors Registry, for the sake of uniformity.

The book is especially recommended for residents and those preparing for board examinations in the fields of orthopedics and radiology. It should form a good base for initial study and a final review.

A Course in Practical Therapeutics. By Martin Emil Rehfuss, M.D., F.A.C.P., Professor of Clinical Medicine and Sutherland M. Prevost Lecturer in Therapeutics, The Jefferson Medical College, Philadelphia; and Alison Howe Price, A.B., M.D., Associate Professor of Medicine, The Jefferson Medical College, Philadelphia. Second edition. 938 pages, illustrated. Baltimore: The Williams and Wilkins Company, 1951. Price $15.00.

This remarkable textbook is the outcome of the authors' course in therapeutics, and it should provide the student with a firm foundation in this discipline.

The first section deals with the diagnostic and therapeutic approach to the patient, and with general therapeutic principles, particularly prescription writing. Many of the better proprietary preparations are recognized throughout the text, but the potentialities of writing compound prescriptions are justly emphasized. The second part of the book, "Symptomatic Therapy," is prob-

ably the most valuable. Treatment of some thirty important symptoms is outlined in detail, and the article on "fever" included in this edition should prove very helpful in the management of this symptom and the diagnosis of cryptogenic fevers. Everywhere, the authors have made use of artistic illustrations to amplify the text.

The third part, comprising the bulk of the volume, is devoted to a condensed description of the differential diagnosis and treatment of most specific medical disorders with the exception of the nervous system. There is a profusion of tables, figures, diets, and discussions of subjects of special interest, such as vagotomy, anticoagulants, and antabuse® therapy. A very worth-while chapter is that on the menopausal syndrome, with an evaluation of hormone treatment. The final section contains a brief outline of important steps in therapy in some of the medical specialties. This includes a very good chapter on pediatric therapy and infant feeding.

This volume has been written from a didactic point of view. Printing and publishing are exemplary. It can be highly recommended as a textbook which will retain its usefulness to the student for many years after graduation.

Bamford's Poisons, Their Isolation and Identification. By C. P. Stewart, D. Cs., Ph.D., Reading in Clinical Chemistry, University of Edinburgh, and Senior Biochemist, Royal Infirmary, Edinburgh. Third edition. 316 pages with 23 illustrations. Philadelphia: The Blakiston Company, 1951. Price $5.50.

This book on toxicologic analysis is intended as a practical laboratory manual for chemists who are investigating cases of poisoning. While emphasis has been placed on details of analytical procedure, much descriptive matter is also included. A review of the pharmacologic and toxicologic effects of many organic poisons, especially the alkaloids of the opium, atropine, cocaine, and ergot groups, will be of interest to the physician. The wide experience acquired by the authors in Egypt is reflected in the chapter on "Drugs of Addiction."

In this new edition, minor changes have been made; the section on barbiturates has been altered because of their increasing importance in toxicology; and a section on antihistamines has been added. The book is well organized, comprehensive, and authoritative. It should be in all collections on forensic medicine and chemistry.

Dynamic Psychiatry, Basic Principals. Volume I. By Louis S. London, M.D., Private Practice Consultant for thirty years in New York City. First edition, 98 pages. New York: Corinthian Publications, Inc., 1952. Price $2.00.

This is an interesting though rather small volume, but the reader soon feels that it does not go far enough. Although the title clearly states it concerns merely basic principals, it is rather sketchily done, and fails to add much that has not been written many times before and just as well.

Perhaps the first chapter, "The Evolution of Psychotherapeutics," is more comprehensive than the rest of the book, but this does not develop anything of practical interest. The recital of so much archaic material concerning the interpretation of dreams detracts from the practical application of dream interpretation and their symbolic content.

The remainder of the book is in kind, which leaves the reviewer with the feeling that it is a nice book, but one which the author enjoyed doing as an amusing task rather than one from which the reader can gain new data.

Factors Regulating Blood Pressure. Transactions of the Fifth Conference, February 15-16, 1951, New York, New York. Edited by Benjamin W. Zweifach and Ephraim Shorr, Department of Medicine, Cornell University Medical College, New York, New York. 238 pages, illustrated. Packanack Lake, New Jersey: Josiah Macy, Jr. Foundation Publications, 1951. Price $3.75.

With the publication of the fifth volume in the series, "Factors Regulating Blood Pressure," the transactions of the Josiah Macy, Jr. Foundation dealing with this subject are concluded. This final volume deals with current investigations in the realm of hypertension and arteriosclerosis, with considerable emphasis on the biochemical and biophysical factors of possible significance in the genesis of arteriosclerosis. Studies among patients on low fat diets, due to famine or to national habit are also discussed. This volume is provided with a cumulative index which makes it particularly valuable to investigators in the field, as well as to physicians interested in current trends of research relative to this all important clinical problem.

Conference on Problems of Aging. Transactions of the Thirteenth Conference, February 5-6, 1951, New York, New York. Edited by Nathan W. Shock, Chief, Section on Gerontology, National Heart Institute, National Institutes of Health and the Baltimore City Hospitals, Baltimore, Maryland. 194 pages, illustrated. Packanack Lake, New Jersey: Josiah Macy, Jr. Foundation Publications, 1951. Price $4.00.

The Thirteenth Conference on "Problems of Aging" published under the auspices of the Josiah Macy, Jr. Foundation records a number of diverse topics such as the endocrine and cardiovascular aspects of aging, the aging of the skin, biology of cell division, and a summary of Federal agencies interested in this increasingly important socio-economic and medical subject. Many of the discussions of necessity go far beyond the problem of aging itself and embrace the broader aspects of cellular metabolism as a whole. As is inevitable in the course of such conferences, many more new questions and ideas are brought forth than are answered or confirmed, but discussion itself is free and uninhibited. Clinicians will find particularly stimulating the discussion dealing with mechanisms of cerebral hemorrhage, and theories regarding the greater longevity of the female of many species.

Adrenal Cortex. Transactions of the Second Conference, November 16-17, 1950. Edited by Elaine P. Ralli, Department of Medicine, College of Medicine, New York University, New York, New York. 209 pages, illustrated. Packanack Lake, New Jersey: Josiah Macy, Jr. Foundation Publications, 1951. Price $3.00.

The publication of the "Transactions of the Second Conference on the Adrenal Cortex" by the Josiah Macy, Jr. Foundation makes available to physicians, physiologists, and pharmacologists a wealth of recently acquired findings relative to the behavior of adrenal steroids. Although investigations with purified adrenal hormones have been going on for more than a decade, widespread interest has arisen relatively recently. The present volume is devoted to considerations of both academic and clinical interest. The five subjects are: present status of chemistry of ACTH, relation of adrenal cortical hormones to hypersensitive states, hyaluronidase and adrenal cortical hormones, and clinical studies with ACTH and adrenal cortical hormones. Despite the experience of each of the participants in this field, there is far from unanimity of opinion. Brought out in these discussions are newer views on the treatment of Addison's disease, findings in hypertensive patients subjected to total adrenalectomy, the degree of purity of ACTH preparations, and differences in influences of DCA and cortisone on water and electrolyte metabolism. This book should prove stimulating to those interested in current concepts in this field.

The Architecture of Normal and Malformed Hearts. By Dr. Alexander Spitzer. Translated and summarized by Maurice Lev, M.D., Associate Professor of Pathology, University of Illinois, College of Medicine; and Aloysius Vass, M.D., Consultant Pathologist, Veterans Administration Hospital, Poplar Bluff, Missouri. 144 pages with illustrations. Springfield, Illinois: Charles C. Thomas, Publisher, 1951. Price $5.00.

Since congenital anomalies of the heart are now very significant from a surgical point of view, a translation of this important embryologic treatise by the Viennese anatomist, Dr. Spitzer, will be received with considerable interest. The monograph contains Spitzer's theories of the normal development of the human heart, and of its abnormal development in cardiac malformations, especially transposition. Basically, these theories apply Haeckel's recapitulation law to the embryologic development of the human heart. In the pathogenesis of transposition, Spitzer postulates an arrest in development at a lower phylogenetic level, with adaptation of the remaining normal structures to the malformed parts. Study of this treatise should prove to be extremely helpful to those interested in congenital cardiac defects. The translation is good, though somewhat literal. The translators have added a clear summary and analysis of Spitzer's thesis, as well as a synopsis of certain criticisms, and a modification proposed by two American workers. There is also a biographic note on the brilliant author, who spent his last days in a concentration camp.

Books Received

The American Journal of Tropical Medicine and Hygiene. Combining The American Journal of Tropical Medicine and The Journal of the National Malaria Society. Official Organ of The American Society of Tropical Medicine and Hygiene. Editor-in-Chief, L. W. Hackett, School of Public Health, University of California, Berkeley, California. Published bimonthly. Baltimore: The Williams and Wilkins Company, 1952.

Cowdry's Problems of Aging: Biological and Medical Aspects. Third edition, edited by Albert I. Lansing, Ph.D., Washington University School of Medicine, St. Louis, Missouri. 1021 pages, illustrated. Baltimore: The Williams & Wilkins Company, 1952. Price $15.00.

Principles of Refraction. By Sylvester Judd Beach, A.B., M.D., F.A.C.S., Consultant, Staff Maine Eye and Ear Infirmary. 157 pages, illustrated. St. Louis: The C. V. Mosby Company, 1952. Price $4.00.

Bone Tumors. By Louis Lichtenstein, M.D., Senior Pathologist, General Medical and Surgical Hospital, Veterans Administration Center, Los Angeles. 315 pages with 155 illustrations. St. Louis: The C. V. Mosby Company, 1952. Price $10.50.

Fundamentals of Psychiatry. By Edward A. Strecker, M.D., Sc.D., LL.D., Litt.D., F.A.C.P., Professor of Psychiatry and Chairman of the Department, Undergraduate and Graduate Schools of Medicine, University of Pennsylvania, Philadelphia. Fifth edition. 250 pages. Philadelphia: J. B. Lippincott Company, 1952. Price $4.50.

Elementary Medical Statistics. The Principles of Quantitative Medicine. By Donald Mainland, M.B., Ch.B., D.Sc., F.R.S.E., F.R.S.C., Professor of Medical Statistics, Division of Medical Statistics, the Department of Preventive Medicine, New York University College of Medicine, New York, New York. 327 pages with 23 illustrations. Philadelphia and London: W. B. Saunders Company, 1952. Price $5.00.

Textbook of Pharmacology. Principles and Application of Pharmacology to the Practice of Medicine. By William T. Salter, M.D., Professor of Pharmacology, Yale University School of Medicine, New Haven, Connecticut. 1,240 pages with 284 illustrations. Philadelphia and London: W. B. Saunders Company, 1952. Price $15.00.

Diabetes and Pregnancy. By Ralph A. Reis, B.S., M.D., F.A.C.S., Professor, Obstetrics and Gynecology, Northwestern University Medical School; Edwin J. DeCosta, B.S., M.D., F.A.C.S., Assistant Professor, Obstetrics and Gynecology, Northwestern University Medical School; and M. David Allweiss, B.S., M.D., Associate in Medicine, Northwestern University Medical School, Chicago, Illinois. 77 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1952. Price $2.50.

Between Two Worlds: The Memoirs of a Physician. By Benjamin L. Gordon, M.D. 354 pages. New York: Bookman Associates, 1952. Price $4.00.

Foundations of Neuropsychiatry. By Stanley Cobb, A.B., M.D., Bullard Professor of Neuropathology, Harvard Medical School. Fifth Revised and Enlarged Edition of the work formerly known as A Preface to Nervous Disease. 287 pages, illustrated. Baltimore: The Williams & Wilkins Company, 1952. Price $3.00.

The Diagnosis of Nervous Diseases. By the Late James Purves-Stewart, K.C.M.G., C.B., M.D. Edin., F.R.C.P., Consulting Physician to Westminster Hospital to the West End Hospital for Nervous Diseases and to the Royal National Orthopaedic Hospital, and C. Worster-Drought, M.A., M.D., Cantab., F.R.C.P., Physician to the West End Hospital for Nervous Diseases. Tenth edition. 962 pages, illustrated. Baltimore: The Williams & Wilkins Company, 1952. Price $10.00.

Medical Disorders of the Locomotor System Including the Rheumatic Diseases. By Ernest Fletcher, M.A., M.D. (Cantab.), M.R.C.P., Physician-in-Charge of the Department of Rheumatism and Lecturer on the Rheumatic Diseases, Royal Free Hospital. Second edition, 888 pages, illustrated. Baltimore: The Williams & Wilkins Company, 1951.

The Quiet Art. A Doctor's Anthrology. Compiled by Dr. Robert Coope. 283 pages. Baltimore: The Williams & Wilkins Company, 1952. Price $3.00.

Ear, Nose and Throat Diseases. For the General Practitioner. By William McKenzie, M.B., B.Chir. (Cantab.), F.R.C.S. (Eng.), Surgeon, Royal National Throat Nose and Ear Hospital; Surgeon, Ear, Nose and Throat Department, Prince of Wales Hospital, Tottenham. 133 pages. Baltimore: The Williams & Wilkins Company, 1952. Price $2.00.

Physiological Changes in Plasma Proteins Characteristic of Human Reproduction. Cross-Sectional and Longitudinal Electrophoretic Data for Women During and Following Uncomplicated and Complicated Pregnancies. By Icie G. Macy, Ph.D., Sc. D., Director of the Research Laboratory, Children's Fund of Michigan, Detroit, and Harold C. Mack, M.D., Department of Obstetrics and Gynecology, Harper Hospital, Detroit. 170 pages. Detroit: Children's Fund of Michigan, 1952.

Bacitracin. A Review and Digest of the Literature up to and Including January, 1952. 127 pages. New York: Research Division, S. B. Penick & Company, 1952.

Advances in Pediatrics. Edited by S. Z. Levine, Cornell University Medical College, New York; and Associate Editors. Volume 5, 273 pages. Chicago: Year Book Publishers, Inc., 1952. Price $7.00.

Hemifacial Spasm. A Clinical and Pathophysiological Study. By Robert Wartenberg, M.D. Foreword by Macdonald Critchley, M.D. 86 pages, illustrated. New York: Oxford University Press, 1952. Price $4.00.

Functional Endocrinology. From Birth through Adolescence. By Nathan B. Talbot, M.D., Associate Professor of Pediatrics, Harvard University; Edna H. Sobel, M.D., Instructor in Pediatrics, University of Cincinnati College of Medicine; Janet W. McArthur, M.D., Instructor in Gynecology, Harvard University; and John D. Crawford, M. D., Instructor in Pediatrics, Harvard University. 638 pages, illustrated. Cambridge, Massachusetts: Harvard University Press, 1952. Price $10.00.

Dynamic Psychiatry. Transvestism, Desire for Crippled Women. By Louis S. London, M.D., Volume 2. 129 pages, illustrated. New York: Corinthian Publications, Inc., 1952. Price $2.50.

Diagnostic Electroencephalography. By Hans Strauss, M.D., Associate in Neurology in Charge of Electroencephalography, Mount Sinai Hospital and Hospital for Joint Diseases, New York City; Mortimer Ostow, M.D., Med. Sc.D., Adjunct in Neurology in Charge of Electroencephalography, Beth Israel Hospital; Adjunct in Neurology for Electroencephalography, Mount Sinai Hospital, New York City; and Louis Greenstein, M.D., Adjunct in Neurology for Electroencephalography, Mount Sinai Hospital, New York City. 282 pages, illustrated. New York: Grune & Stratton, 1952. Price $7.75.

Diseases of the Nose, Throat and Ear. A Handbook for Students and Practitioners. By I. Simson Hall, M.B., Ch.B., F.R.C.P.E., F.R.C.S.E., Surgeon to the Royal Infirmary, Edinburgh (Department for Diseases of Nose, Throat and Ear); Lecturer in Diseases of Nose, Throat and Ear, University of Edinburgh. Fifth edition. 463 pages, illustrated. Baltimore: The Williams and Wilkins Company, 1952. Price $4.00.

New Outlook on Mental Diseases. By F. A. Pickworth, M.B., B.Sc., B.Sc., Consultant Pathologist, Group 6 Hospital, Birmingham; Formerly Director, Joint Board of Research for Mental Disease, City and University of Birmingham, England. 296 pages. Baltimore: The Williams and Wilkins Company, 1952. Price $12.00.

A Synopsis of Neurology. By W. F. Tissington Tatlow, M.D., M.R.C.P. (Lond.), Medical Registrar, Maida Vale Hospital for Nervous Diseases, London; J. Amor Ardis, M.B., Ch.B., D.P.M. (Brist. and Lond.), Senior Registrar in Psychiatry, Aberdeen General and Mental Hospitals; and J. A. R. Bickford, M.R.C.S., L.R.C.P.; D.P.M. (Brist.), Senior Registrar in Psychiatry, Maryfield Hospital, Dundee and Dundee Mental Hospital, Gowrie House. 513 pages, illustrated. Baltimore: The Williams and Wilkins Company, 1952. Price $6.50.

Cybernetics. Circular Causal and Feedback Mechanisms in Biological and Social Systems. Transactions of the Eighth Conference, March 15-16, New York, New York. Edited by Heinz von Foerster, Department of Electrical Engineering, University of Illinois, Champaign, Illinois. Assistant Editors, Margaret Mead, American Museum of Natural History, New York, New York, and Hans Lukas Teuber, Department of Neurology, New York University College of Medicine, New York, New York. 240 pages. Packanack Lake, New Jersey: Josiah Macy, Jr. Foundation Publications, 1952. Price $4.00.

Cold Injury. Transactions of the First Conference, June 4-5, 1951, New York, New York. Edited by M. Irene Ferrer, Department of Medicine, College of Physicians and Surgeons, Columbia University, New York, New York. 248 pages, illustrated. Packanack Lake, New Jersey: Josiah Macy, Jr. Foundation Publications, 1952. Price $3.25.

Southern Medical News

ALABAMA

Medical Association of the State of Alabama, at its meeting held in Montgomery, April 17-19, installed Dr. B. W. McNease, Fayette, president; and elected Dr. James O. Morgan, Gadsden, president-elect; Dr. T. J. Payne, Jasper, vice-president; and as board members, Dr. Robert Parker, Montgomery, and Dr. J. G. Daves, Cullman.

A bronze bust of the late Dr. Lloyd Noland was unveiled recently at the Lloyd Noland Hospital, Fairfield. The bust will be placed on the grounds of the hospital in memory of this physician who served as the hospital's director from its start in 1919 until his death in 1949.

Alabama Association of Pathologists, at a recent meeting, elected Dr. J. S. Peter Beck, Tuscaloosa, president; Dr. Earl B. Wert, Mobile, vice-president; and Dr. W. F. Scott, Jr., Birmingham, secretary. Dr. J. D. Bush, Gadsden, the retiring president, was appointed chairman of the executive committee.

Mobile County Chapter of the Academy of General Practice has installed Dr. George W. Neburn, Jr., president, elected Dr. V. H. Hill, president-elect; and reelected Dr. F. T. England, vice-president; Dr. William G. Fonde, secretary; and Dr. B. B. Kimbrough, treasurer.

Dr. William A. Cunningham, Birmingham, is Chairman of the membership committee of the American Committee on Maternal Welfare of the American Congress on Obstetrics and Gynecology. His committee will study existing maternal welfare organizations not now affiliated with the American Committee, preliminary to inviting such groups to become members.

ARKANSAS

Dr. R. B. Robins, Camden, was elevated to the presidency of the American Academy of General Practice at its meeting held in Atlantic City in March.

Dr. W. T. Holman, Jr., Van Buren, has been elected a director of the Van Buren Business and Professional Association.

DISTRICT OF COLUMBIA

Aero Medical Association at its meeting held in Washington in March installed Dr. William R. Stovall, president; and elected Dr. Bertram Groesbeck, Jr. (Rear Admiral, MC, USN), vice-president, both of Washington.

Dr. Roger M. Choisser, professor of pathology, George Washington University School of Medicine, Washington, who has been a member of the University staff over a period of thirty-one years, received the George Washington University Medical Society's annual Award of Merit at a recent meeting of the Society.

Dr. Sol Katz and Dr. William S. McCune, both of Washington, have been added as associate editors of *GP*, the official publication of the American Academy of General Practice.

Dr. Robert B. Nelson, who is on the staff of Garfield, Doctors, Columbia, and Emergency Hospitals, Washington, has recently assumed the position of Medical Director of Planned Parenthood Association of the District of Columbia.

Dr. J. DeWitt Fox, Washington, Editor of *Life and Health*, was one of a group of ten representatives of the medical, dental and allied professions chosen from over the nation to observe treatment given wounded servicemen aboard hospital ships en route home from Korea.

Dr. Theodore A. Guenther, chief anesthesiologist, Georgetown University Hospital, Washington, since the resignation of Dr. Edward B. Tuohy last November, has resigned to enter private practice in Cincinnati, Ohio.

Dr. Oliver P. Winsley, Jr., has moved from Washington to Coral Gables, Florida.

FLORIDA

Florida Medical Association, at its annual meeting held in Hollywood, April 29-30, installed Dr. Robert M. McIver, Jacksonville, president; elected Dr. Frederick K. Herpel, West Palm Beach, president-elect; Dr. Francis F. Langley, St. Petersburg, first vice-president; Dr. Erasmus Hardee, Vero Beach, second vice-president; Dr. H. Q. Jones, Fort Myers, third vice-president; and reelected Dr. Samuel M. Day, Jacksonville, secretary-treasurer; and Dr. Shaler Richardson, Jacksonville, editor of the *Journal of the Florida Medical Association*.

Dr. Warren W. Quillian, Coral Gables, as president, presided over the American Academy of Pediatrics at the meeting held in Washington, Hotel Statler, May 22-24.

Dr. M. Jay Flipse, Miami, is Regent of the American College of Chest Physicians for the district and Dr. Clarence M. Sharp, Jacksonville, governor of the College for Florida. Officers of the Florida Chapter of the College are Dr. Howard K. Edwards, president; and Dr. Nathaniel M. Levin, secretary-treasurer, both

Continued on page 30

as an antihistaminic agent

Pyribenzamine® *is unsurpassed*

in allergic rhinitis . . .

in urticaria

in serum sickness

in angioneurotic edema

in hay fever

in drug reactions

for maximal relief

with minimal side effects

Pyribenzamine hydrochloride
(brand of tripelennamine hydrochloride)

Ciba Pharmaceutical Products, Inc., Summit, N. J.

Ciba

2/17209M

Continued from page 580

of Miami. The eighteenth annual meeting of the American College of Chest Physicians will be held in Chicago, Congress Hotel, June 5-8.

Dr. Benjamin F. Barnes, Chattahoochee, was recently presented a plaque by the Woodmen of the World in recognition of his outstanding service as a doctor and citizen in Chattahoochee for the past fifty years.

Dr. Paul F. Hutchins, Jacksonville, is at Tulane University School of Medicine, New Orleans, for a year's study in orthopedic surgery and adult reconstruction.

Dr. Warren Lindau has opened an office in Coral Gables for the practice of internal medicine.

Dr. Fred L. Adair, Maitland, who has been president of the American Committee on Maternal Welfare of the American Congress on Obstetrics and Gynecology since it was incorporated in 1934, is succeeded by Dr. Frederick H. Falls, Chicago. Dr. Adair was one of the founders and key figures of the Joint Committee on Maternal Welfare, formed in 1919, which eventually broadened into the present organization.

GEORGIA

Medical Association of Georgia, at its annual meeting held in Atlanta, May 11-14, installed Dr. C. F. Holton, Savannah, president; and elected Dr. William P. Harbin, Jr., Rome, president-elect; Dr. Rudolph Bell, Thomasville, first vice-president; Dr. James H. Semans, Atlanta, second vice-president; and Dr. David Henry Poer, Atlanta, secretary-treasurer.

The Better Health Council of Georgia has been organized as an outgrowth of the Georgia Citizens Council which was supported by the state. The purpose of the new organization is to promote better health in Georgia, to organize regional health conferences and local health councils, and to promote coordination of various health agencies. It is now supported by the State Association, the Medical College of Georgia, Emory University School of Medicine, Georgia Dental Association, Emory University School of Dentistry, Georgia State Nurses Association, State Department of Health and private health agencies.

Dr. Charley K. Wall, Thomasville, has been appointed to fill the unexpired term of the late Dr. Steve P. Kenyon, Dawson, as a member of the State Board of Medical Examiners.

KENTUCKY

Kentucky State Medical Association will hold its next annual meeting in Louisville, October 7-9. This meeting will be dedicated to the memory of Dr. Daniel Drake, one of the first honorary members of the Kentucky State Medical Association.

Dr. Clark Bailey, Harlan, President of the Kentucky State Medical Association, has been appointed to serve on the American Medical Association Committee on Legislation, which considers all legislation that concerns the health of the nation.

The Tri-City meeting of the Cincinnati, Indianapolis and Louisville Obstetrical and Gynecological Societies was held in February with the Louisville Society as host.

The program for the first Telephone Seminar in Kentucky was arranged by Dr. Robert L. Lich and Dr. Herbert L. Clay, Louisville, director of postgraduate training at the University of Louisville School of Medicine. Panelists for this seminar, were: Dr. William M. Christopherson, assistant professor of pathology at the School; Dr. Walter S. Coe, assistant professor of medicine, moderator; Dr. J. Murray Kinsman, dean of the University of Louisville School of Medicine, who introduced the panel; Dr. Marion F. Beard, associate professor of medicine, chief of Hematology Section; and Dr. George B. Sanders, assistant professor of surgery.

Dr. Walter B. Grenell, Union City, Tennessee, has taken over the Haws Memorial Hospital, Fulton.

Dr. John G. Coleman, who has just completed a tour of duty in the Armed Service, has located at Lexington, practice limited to surgery.

Dr. Bessie Lee Allnutt, a 1949 graduate of the University of Cincinnati College of Medicine, has located at Covington.

LOUISIANA

A Southern regional research conference of the American Psychiatric Association and the Department of Psychiatry, Tulane University School of Medicine, New Orleans, was held at the medical school building in March with more than fifty psychiatrists in the Southern region of the United States taking part.

Dr. Guy A. Caldwell, professor of orthopedic surgery, Tulane University School of Medicine, New Orleans, has resigned from

Continued on page 36

THE NEW YORK POLYCLINIC

MEDICAL SCHOOL AND HOSPITAL

(ORGANIZED 1881)

(The Pioneer Post-Graduate Medical Institution in America)

OBSTETRICS and GYNECOLOGY

A full-time course. In Obstetrics: lectures; prenatal clinics; witnessing normal and operative deliveries; operative obstetrics (manikin). In Gynecology: lectures; touch clinics; witnessing operations; examination of patients preoperatively; follow-up in wards postoperatively. Obstetrical and gynecological pathology. Anesthesia. Attendance at conferences in obstetrics and gynecology. Operative gynecology on the cadaver.

COURSE FOR GENERAL PRACTITIONERS

Intensive full-time instruction covering those subjects which are of particular interest to the physician in general practice. Fundamentals of the various medical and surgical specialties designed as a practical review of established procedures and recent advances in medicine and surgery. Subjects related to general medicine are covered and the surgical departments participate in giving fundamental instructions in their specialties. Pathology and radiology are included. The class is expected to attend departmental and general conferences.

SURGERY and ALLIED SUBJECTS

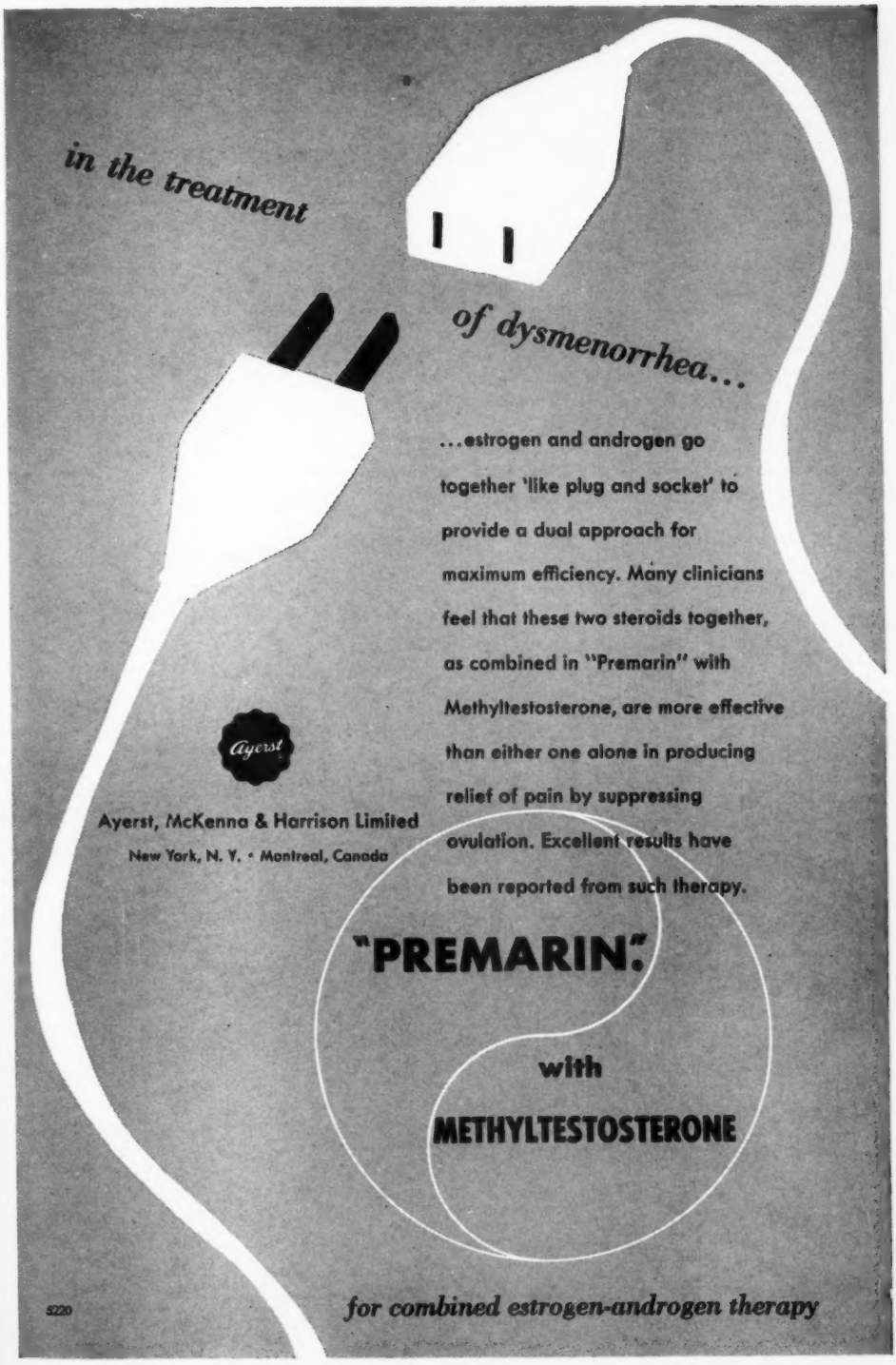
A combined surgical course comprising general surgery, traumatic surgery, abdominal surgery, gastroenterology, proctology, gynecological surgery, urological surgery. Attendance at lectures, witnessing operations, examination of patients preoperatively and postoperatively and follow-up in the wards postoperatively. Pathology, radiology, physical medicine, anesthesia. Cadaver demonstrations in surgical anatomy, thoracic surgery, proctology, orthopedics. Operative surgery and operative gynecology on the cadaver; attendance at departmental and general conferences.

ANESTHESIA

A three months full-time course covering general and regional anesthesia, with special demonstrations in the clinics and on the cadaver of caudal, spinal, field blocks, etc.; instruction in intravenous anesthesia, oxygen therapy, resuscitation, aspiration bronchoscopy; attendance at departmental and general conferences.

For Information about these and other courses Address

THE DEAN, 345 WEST 50TH STREET, NEW YORK 19, N. Y.


in the treatment
of dysmenorrhea...
...estrogen and androgen go together 'like plug and socket' to provide a dual approach for maximum efficiency. Many clinicians feel that these two steroids together, as combined in "Premarin" with Methyltestosterone, are more effective than either one alone in producing relief of pain by suppressing ovulation. Excellent results have been reported from such therapy.
Ayerst
Ayerst, McKenna & Harrison Limited
New York, N. Y. • Montreal, Canada
"PREMARIN"
with
METHYLTESTOSTERONE
5220
for combined estrogen-androgen therapy

IT WAS A BRIGHT EARLY DECEMBER DAY and Lieutenant Hudner was flying a Korean combat mission alongside another plane piloted by Ensign Jesse Brown. A burst of flak caught the ensign's plane and he went spinning down, aflame. Despite the presence of enemy ground troops, Lieutenant Hudner then deliberately crash landed near his flame-trapped shipmate. He radioed for help, after which he fought to keep the fire away from the fatally injured ensign until a rescue helicopter arrived. Today Lieutenant Hudner has something to say to you:

"Maybe if America had been strong enough to discourage aggression two years ago, my friend, Jesse Brown, might be alive right now. So might thousands more of our Korea dead.

"For it's only too sadly true—today, in our world, weakness invites attack. And *peace is only for the strong.*

"Our present armed forces *are* strong—and growing stronger. But don't turn back the clock! Do your part toward *keeping* America's guard up by buying more . . . and more . . . and more United States Defense Bonds *now!* Back us up. And *together* we'll build the strong peace that all Americans desire!" *Peace is for the strong! Buy U. S. Defense Bonds now!*

★ ★ ★

Remember that when you're buying bonds for defense, you're also building a reserve of savings. Remember, too, that if you don't save *regularly*, you generally don't save at all. So sign up today in the Payroll Savings Plan where you work, or the Bond-A-Month Plan where you bank. For your country's security, and your own, buy U. S. Defense Bonds now!

Lieutenant (jg)
Thomas Hudner, Jr.
U.S.N.

Medal of Honor

The U. S. Government does not pay for this advertisement. It is donated by this publication in cooperation with the Advertising Council and the Magazine Publishers of America.

a successful New product

in the treatment of allergies and dermatoses

Pyromen®

(BACTERIAL POLYSACCHARIDE)

Pyromen initiates responses in the circulating leucocytes and in the reticulo-endothelial system.

Pyromen is proving to be increasingly useful in the treatment of many allergies and dermatoses, as well as certain ophthalmic disorders.

Pyromen is supplied in 10 cc. vials containing 4 gamma (micrograms) per cc. and in 10 cc. vials containing 10 gamma per cc.

"***Pyromen***" on your *Rx* will bring you our new booklet detailing the use of this new therapeutic agent.

Manufactured by

TRAVENOL LABORATORIES, INC.

Subsidiary of BAXTER LABORATORIES, INC.
Morton Grove, Illinois

calm

the turbulent colon

in Summer diarrhea

with

DIABISMUL

Pink

(TILDEN)

- absorbent, soothing, mildly astringent
- protects irritated intestinal mucosa against further injury
- helps consolidate the stool, and diminish fluid loss, and thus . . .
- aids in restoring normal peristalsis

DIABISMUL Pink is a superior anti-diarrheal suspension containing considerably more Bismuth Subsalicylate per ounce than the usual preparations.

	per fluid ounce	per 100 cc.
Paregoric	60 min	12.5 cc.
Bismuth Subsalicylate	8 gr.	1.750 Gm.
Salol	1 3/5 gr.	0.350 Gm.
Zinc Phenolsulfonate	4/5 gr.	0.175 Gm.

Supplied in pint and gallon bottles.

Write for samples—giving narcotic registry number.

our new Address:

The TILDEN Company

435 Chestnut Street

CHATTANOOGA 2, TENN.

Home Office: New Lebanon, N. Y.

Continued from page 30

the chairmanship of the Department of Orthopedics but will continue in the professorial rank. He is succeeded by Dr. Jack W. Wickstrom, associate professor of orthopedic surgery since 1945.

Dr. Russell L. Holman, professor and head, Department of Pathology, Tulane University School of Medicine, New Orleans, has been appointed consultant to the Division of Biology and Medicine of the Atomic Energy Commission.

Dr. W. P. Gardiner, New Orleans, has been presented a certificate of merit and a key to the city in recognition of the city being placed on the honor roll of the U. S. Public Health Service for high milk ratings.

MARYLAND

The spring scientific meeting of the Maryland Academy of General Practice was held in Hagerstown, May 15.

Dr. Nicholson J. Eastman, Baltimore, is head of the Research Committee of the American Committee on Maternal Welfare which will direct allocation of funds from the Fred Lyman Adair Foundation, a foundation set up in 1950 to promote research and improve education in the maternal welfare fields.

Drs. George W. Anderson, Trent Busby and Robert Nesbitt, Johns Hopkins Hospital, Baltimore, won third place for their scientific exhibit, "Pathology of Perinatal Death," at the Fifth American Congress on Obstetrics and Gynecology held in Cincinnati, Ohio, recently.

Dr. Alan F. Guttmacher, Baltimore, a former president of the Obstetrical and Gynecological Society of Maryland and Chief, Department of Obstetrics, Sinai Hospital, was recently tendered a farewell dinner by the Society and the hospital staff. He will be director of obstetrics and gynecology at the Mt. Sinai Hospital, New York City.

MISSISSIPPI

Greenwood Hospital, Greenwood, a 135-bed hospital, was recently opened. The members of the medical staff are: Drs. G. Y. Gillespie, chief, J. C. Adams, J. M. Alford, George Baskerville, I. B. Bright, S. L. Brister, John Lucas, E. M. Meek, George Nasser, H. A. Nelson, L. B. Otken, J. C. Pegues, Fred Sandifer and R. E. Wilson.

Dr. James Grant Thompson, Jackson, a member of the State Medical Education Board by virtue of his office as president of the Mississippi State Medical Association was recently honored when the members of the board paid tribute to him.

MISSOURI

Missouri State Medical Association, at its 94th annual meeting held in St. Louis, March 30-April 2, installed Dr. J. William Thompson, St. Louis, president; and elected Dr. E. Claude Bohrer, West Plains, president-elect; Dr. Clinton W. Lane, vice-president; and Dr. Charles E. Hyndman, treasurer.

The Hill-Burton Hospital construction in Missouri, reported by the Division of Hospital facilities, FSA, the first of the year: eight projects completed and in operation at a total cost of $6,866,483, including federal contribution of $2,203,848 and to supply 447 additional beds; ten projects under construction at a total cost of $15,939,301, including federal contribution of $7,842,179 and designed to supply 795 additional beds; and one project approved but not yet under construction to cost $36,000, including $180,000 federal contribution and designed to supply 59 additional beds.

The Institute of Biophysics within the Department of Biology and the Graduate School at St. Louis University has been established under the direction of Professor Basile J. Luyet. Three grants have been awarded Professor Luyet to carry on this work, a total of $13,880: $6,120 from the Public Health Service of the Federal Security Agency for a study of "mode of action of Glycerol in the preservation of life in frozen cells"; $3,800 from the Jane Coffin Childs Memorial Fund for Medical Research for "comparative study of the survival of various embryonic and adult tissues after ultra-rapid freezing"; and $3,960 from the National Science Foundation for the study of "survival of vitrified and dried tissues and organisms."

NORTH CAROLINA

Southern Pediatric Seminar will hold its thirty-second session in Saluda, July 14-26. For complete information, write Dr. D. Lesesne Smith, Spartanburg, South Carolina.

Continued on page 36

Dryco *for easy digestion*

So often, the hot summer season brings upset stomachs, fermentative diarrhea, impaired infant digestion . . .

Dryco . . . for 30 years a most readily digested formula for prematures . . . offers your tinier patients valuable help.* Check these advantages:—

LOW IN FAT — LOW IN CARBOHYDRATE
HIGH IN PROTEIN — ENRICHED WITH VITAMINS A AND D
FINE, FLOCCULENT CURD — THE HALF WHOLE, HALF SKIM-MILK MIXTURE

Only vitamin C need be added. Reconstitute Dryco in cold or warm water. Use in a wide range of formulas according to nutritional requirements. Additional data and samples will be mailed on request.

*Gordon, Harry H.: Feeding of Premature Infants, American Journal of Diseases of Children 73:713 (June) 1947.

Dryco®

Each tablespoonful supplies 31½ calories.
Frequently used for supplemental feedings.
Available at pharmacies in 1 and 2½ lb. cans.

Prescription Products Division, The **Borden** Company, *350 Madison Ave., New York 17*

Classified Advertisements

RESIDENT WANTED—Appointments to vacancies in the first and second year program of an approved residency in Internal Medicine are available at the VAH, Coral Gables, Florida. Address Chairman, Deans Committee, Dr. L. G. Rowntree, du-Pont Building, Miami, Florida.

UROLOGIST—32, Board eligible; family; category four; five years approved medical, surgical, urological residency. Desires location for practice, will consider association or clinic. Available August 1, 1952. Reply: Dr. J. M. Beck, 4515 Maplecrest Avenue, Parma, Ohio.

WANTED—Physician for Alabama State Mental Institution. Salary $6,600.00 to $7,800.00. Must be licensed. Contact Steward, Alabama State Hospitals, Tuscaloosa, Alabama.

BUY
U. S. DEFENSE
BONDS

Continued from page 34

The W. D. Bell Medical Research Building, the newest wing on the Duke Medical Research building, Durham, has been completed. It was named in honor of the late W. B. Bell, president of the American Cyanamid Company, who was a trustee of the Duke Endowment. The new cancer and heart research wing, which completes the basic "H-shaped" structure of the building, was constructed with a $200,000 grant from the National Cancer Institute of the U. S. Public Health Service, $44,000 from the National Heart Institute of the USPHS, and $150,000 from Duke University. The first unit of the research building was completed in September, 1947, the second wing two years later, and this third wing, just finished, was begun last year. Dr. Wilburt C. Davison, dean of the Duke Medical School, after 22 years in the Medical School, will have his new quarters in the west part of the wing.

Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, has promoted three faculty members to full professors: Dr. Fred K. Garvey, urology; Dr. James A. Harrill, otolaryngology; and Dr. Robert L. McMillan, clinical internal medicine.

Dr. Bayard Carter, Durham, has been re-elected vice-president of the American Committee on Maternal Welfare of the American Congress on Obstetrics and Gynecology.

Drs. George H. Petteway and Harvey C. May, Charlotte, announce the association of Dr. W. Leslie McLeod in the practice of obstetrics and gynecology.

Dr. William Carl Whitesides, Jr., formerly of York, South Carolina, has located in Charlotte for the practice of internal medicine.

Dr. Glenn S. Edgerton, Charlotte, announces the association of Dr. Harold Sluder in the practice of gynecology and obstetrics.

Dr. McTyeire G. Anders, Gastonia, has been chosen by the Gaston County Medical Society as his county's "Doctor of the Year."

Dr. Thomas R. Huffines and Dr. George G. Gilbert, Asheville, announce the association of Dr. Ralph G. Eaker in the practice of urology.

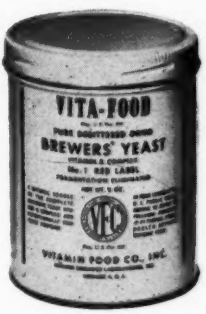
Continued on page 42

OPTIMUM EFFICACY

Dried Brewers' Yeast is, everywhere, the accepted standard for the whole of Vitamin B; in child growth, for the independent vitamin growth factor; for the promotion of lactation; in beri-beri, pellagra; and in disorders due, either in part or in the main, to deficiency in the B vitamins.

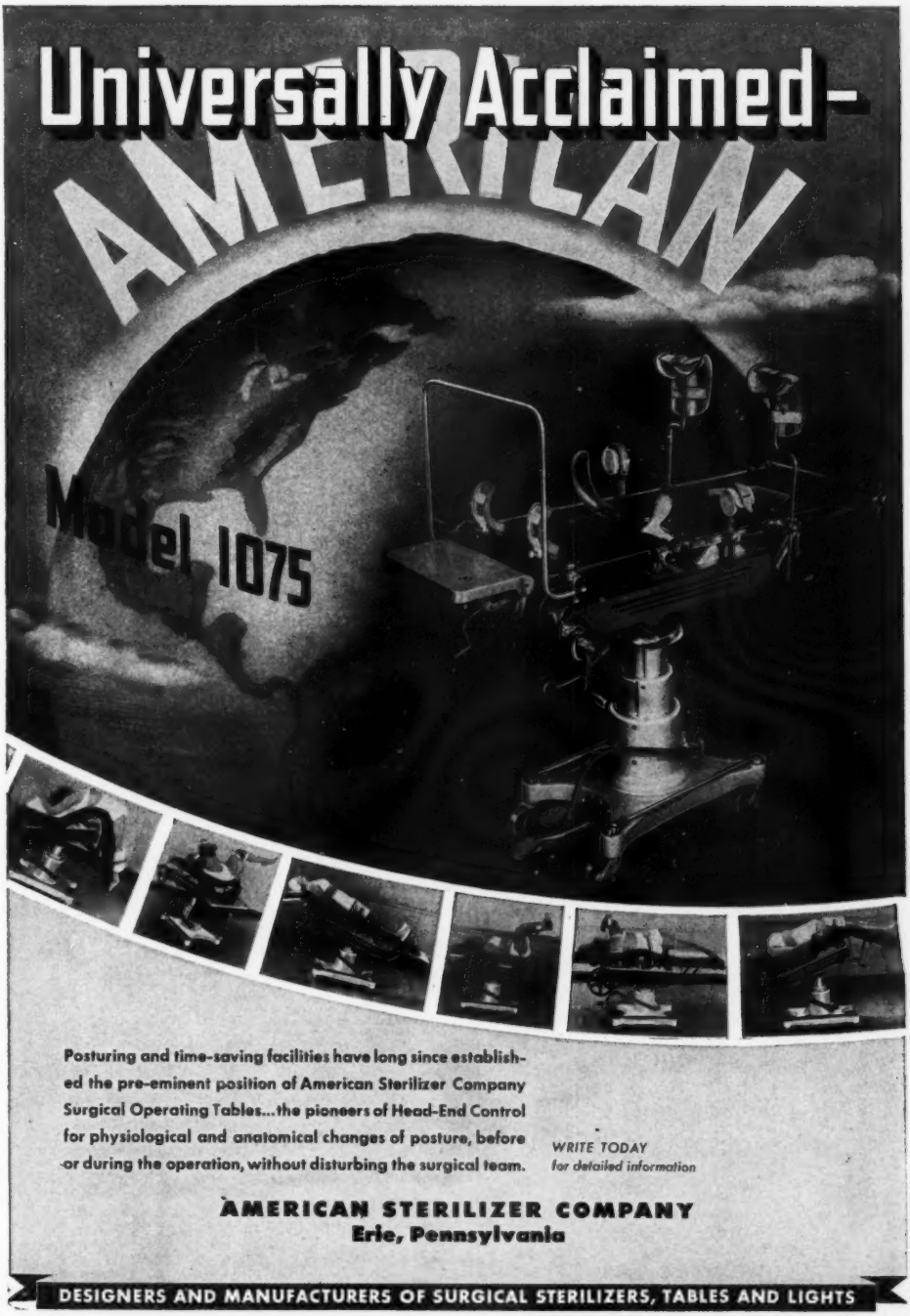
Brilliant work has been done in separating and synthesizing some of the important parts of vitamin B. As yet these parts, singly or together, need the unseparated balance and which in biological assays, nutritional and medical need, Dried Brewers' Yeast supplies.

Where the physician uses one or several of these parts for the temporary therapeutic value, VITA-FOOD genuine brewery grown, whole grain mash origin Dried Brewers' Yeast can be depended upon to supply the missing parts.



VITAMIN FOOD CO. INC.

187 Sylvan Avenue Newark 4, N. J.



Posturing and time-saving facilities have long since established the pre-eminent position of American Sterilizer Company Surgical Operating Tables...the pioneers of Head-End Control for physiological and anatomical changes of posture, before or during the operation, without disturbing the surgical team.

WRITE TODAY
for detailed information

AMERICAN STERILIZER COMPANY
Erie, Pennsylvania

DESIGNERS AND MANUFACTURERS OF SURGICAL STERILIZERS, TABLES AND LIGHTS

Wyeth®

In bacterial diarrheas:

bacteriostasis – adsorption protection

Streptomagma provides all the essentials for securing prompt and complete remission of many bacterial diarrheas. To accomplish these ends Streptomagma contains:

- Streptomycin . . . "much more effective against the coliform fecal flora than the sulfonamides . . . not readily absorbable . . . non-irritating to the mucosa"[1]
- Pectin . . . "various pectins . . . become bactericidal agents in the gastrointestinal tract when given together with streptomycin"[2]
- Kaolin . . . for "tremendous surface and high adsorptive power"[3]
- Alumina gel . . . itself a potent adsorptive, acts as a suspending agent for the kaolin and enhances its action; soothes and protects the irritated intestinal mucosa.

STREPTOMAGMA*

Dihydrostreptomycin sulfate and pectin with kaolin in alumina gel

Wyeth INCORPORATED, Philadelphia 2, Pa.

1. Pulaski, E. J. and Connell, J. F., Jr.: Bull. U. S. Army M. Dept. 9:265.
2. Wooldridge, W. E. and Mast, G. W.: Am. J. Surg. 78:881.
3. Swalm, W. A.: M. Rec. 140:26.

*TRADEMARK

normal activity

for the hypertensive patient

To keep arterial pressure at safe levels, conservative medical management demands a multiple approach---vasodilation, mild diuresis and sedation, and as a prophylactic measure, maintenance of capillary integrity with Rutin and Ascorbic Acid.

The Semhyten formula is designed for this logical multiple approach.

Each capsule contains:

Phenobarbital	1/4 gr.	(15 mg.)
Mannitol Hexanitrate	1/2 gr.	(30 mg.)
Theophylline	1 1/2 gr.	(0.1 Gm.)
Rutin		10 mg.
Ascorbic Acid		15 mg.

Semhyten

S.E.Massengill

Professional literature available. Bristol, Tenn

The Viso-Cardiette started something

Although the direct-writing Viso-Cardiette was introduced, and completely accepted, as a *clinical electrocardiograph,* the eyes of other fields—research, for example—were soon turned to the *surplus* of its clinical recording characteristics, and the wide range of its potentialities.

Research had been asking also for an instrument that would record *more than one* phenomena *simultaneously,* and do so via the *same basic design advantages* of the then already popular Viso-Cardiette. In answer, Sanborn engineers multiplied the Viso-Cardiette by *four,* so to speak, and came up with the four-channel *Poly-Viso* Cardiette—soon to follow it, in the same manner, with the *two*-channel *Twin-Viso* Cardiette.

There were also those who wanted a *less* elaborate instrument than the Viso in that they had no need for 'cardiography, but desired all the recording advantages of a one-channel system. And so, the *lower cost* Viso-Recorder was designed.

Nor was this imposing array of Sanborn recording systems long to go unrecognized in the field of Industry where many recording problems are now being solved "the Viso way."

Taken as a common denominator of all the various Viso models in use today (both medical and industrial), one-channel Sanborn systems now total *nearly 20,000.*

Yes, the Viso-Cardiette really started something!

The Viso-Cardiette was the FIRST Ecg to be accepted by the A.M.A. Council on Physical Medicine and Rehabilitation.

Further information and descriptive literature on the Viso-Cardiette, or Sanborn one-, two-, or four-channel recording systems will gladly be sent on request.

SANBORN CO.
CAMBRIDGE 39, MASSACHUSETTS
Makers of Electrocardiographs Since 1924

NEW 5-mg. Tablets of Cortone®

For accurate adjustment of Maintenance Dosage and for therapy in conditions responding to Low Dosage

RHEUMATOID ARTHRITIS

ADDISON'S DISEASE

ADRENOGENITAL SYNDROME

FOLLOWING BILATERAL ADRENALECTOMY

Advantages of 5-mg. Tablets

FLEXIBILITY—

Used alone or in conjunction with the 25-mg. tablets, the new 5-mg. tablets afford greater flexibility in adjusting dosage to the individual patient's requirements. Fluctuations in the natural course of rheumatoid arthritis may be better controlled.

ACCURACY—

Permit more accurate establishment of minimum maintenance doses, thus controlling symptoms more closely and further minimizing the incidence of undesirable physiologic effects.

ECONOMY—

Prevent waste of CORTONE by more exact correlation between requirement and dosage.

Literature on Request

Cortone*
ACETATE
(CORTISONE ACETATE, MERCK)

*CORTONE *is the registered trade-mark of Merck & Co., Inc. for its brand of cortisone. This substance was first made available to the world by Merck research and production.*

MERCK & CO., INC.
Manufacturing Chemists
RAHWAY, NEW JERSEY
In Canada: MERCK & CO. Limited—Montreal

Continued from page 36

Dr. Charles M. Kendrick and Dr. Frederick A. Thompson, Jr., Lenoir, have opened an office as partners in the practice of internal medicine.

The April, 1952 issue of the *North Carolina Medical Journal* is the William DeBerniere MacNider Memorial issue, a reminder of the life and works of Dr. MacNider. His portrait was painted in 1945 by John C. Johansen and hangs in the medical library of the University of North Carolina at Chapel Hill.

OKLAHOMA

Dr. J. Raymond Hinshaw, a graduate of the University of Oklahoma, is now associated with the Strong Memorial Hospital, Rochester, New York.

Mary Hurley Hospital, Coalgate, is one of the newest hospitals constructed in Oklahoma. It has 39 rooms and was named in memory of Mary Hurley, the mother of General Patrick Hurley.

Dr. O. L. Parsons, Lawton, has been named to the Executive Board of the American Academy of Obstetrics and Gynecology.

Dr. H. E. Barnes has moved from Oklahoma City to Choctaw.

Dr. L. J. Starry, Oklahoma City, has been reelected president and chief of staff of St. Anthony's Hospital, Oklahoma City.

Oklahoma Chapter of the Academy of General Practice at its recent meeting elected Dr. Warren Poole, president; Dr. A. R. Jackson, vice-president; and Dr. Byron E. Williams, secretary-treasurer.

SOUTH CAROLINA

The Association of Surgeons of the Southern Railway System held its fifty-first annual meeting in Charleston, Fort Sumter Hotel, April 28 and 29, under the presidency of Dr. Edward T. Newell, Jr., Chattanooga, Tennessee. Other officers were Dr. William H. Prioleau, Charleston, first vice-president; Dr. J. D. Martin, Jr., Emory University, Georgia, second vice-president; Dr. W. F. Harper, Selma, Alabama, third vice-president; and Dr. J. Marsh Frere, Sr., Chattanooga, Tennessee, recording secretary.

Dr. John M. Preston, medical examiner in charge of tuberculosis services with the regional office of the Veterans Administration in Columbia, assumed duties as Director of the Richland County Health Department on April 1.

South Carolina Chapter of the Academy of General Practice will meet in Clemson, August 19 and 20. Officers are Dr. Thomas G. Goldsmith, Greenville, president; Dr. W. H. Speisseger, Charleston, president-elect; Dr. M. W. Cheatham, Columbia, vice-president; and Dr. Hervey W. Mead, Pendleton, secretary-treasurer.

Dr. John F. McLaughlin, Jr., has opened offices at Meggett for the practice of general medicine.

Medical College of the State of South Carolina, Charleston, after 120 years has resumed by legislative action its original name, the Medical College of South Carolina.

Dr. Harold Pettit is the new co-editor of *The Scribe*, published by the Medical Society of South Carolina and the Charleston County Medical Society. Dr. J. I. Waring, Charleston, is the editor.

TENNESSEE

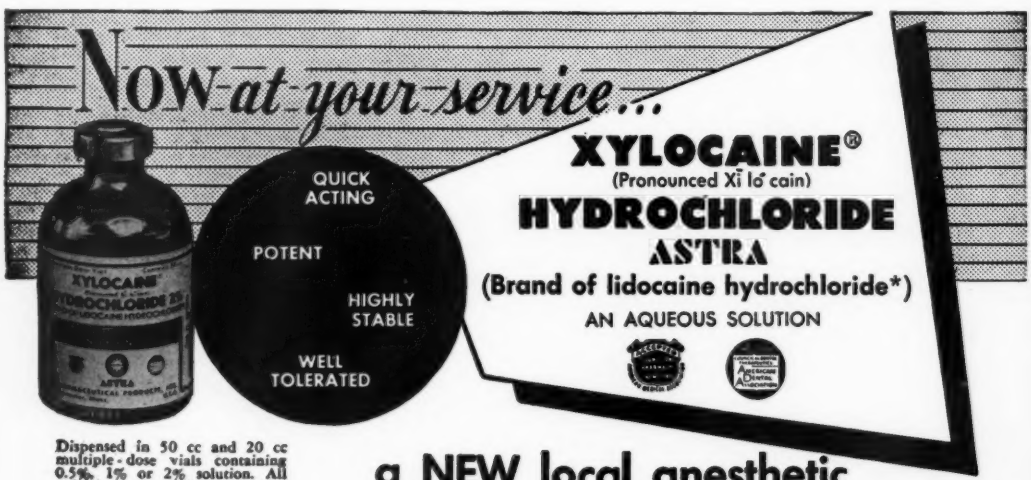
Dr. Edward T. Newell, Jr., Chattanooga, as president, presided over the fifty-first annual meeting of the Association of Surgeons of the Southern Railway System, held at Charleston, South Carolina, April 28 and 29.

Dr. Jere L. Crook, Jackson, continues to improve following a heart attack some time ago, and spends some time in his office each day.

Dr. R. H. Kampmeier, Nashville, Secretary-Editor of the Tennessee State Medical Association, succeeds the late Dr. Herbert Acuff, Knoxville, as a member of the Board of Directors of the Tennessee Hospital Service Association (Blue Cross).

Dr. James D. Hardy, assistant professor of surgery, University of Tennessee College of Medicine, Memphis, has been awarded

Continued on page 46



Dispensed in 50 cc and 20 cc multiple-dose vials containing 0.5%, 1% or 2% solution. All solutions available without epinephrine and with epinephrine 1:100,000. 2% solution also supplied with epinephrine 1:50,000.

STOCKED BY LEADING WHOLESALE DRUGGISTS AND SURGICAL SUPPLY HOUSES.

a NEW local anesthetic

A potent, short-acting local anesthetic, producing on injection, a more prompt, intense and extensive anesthesia than equal concentrations of procaine hydrochloride. Useful and effective either with or without epinephrine, it has been described (1) as the most promising of the new local anesthetics, approaching in efficiency the nerve blocking properties of piperocaine, and in toxicity, the advantages of safety presented by procaine.

(1) Hanson, I. R. and Hingson, R. A., *Current Researches in Anesthesia and Analgesia*, 29:136 (May-June) 1950

ASTRA PHARMACEUTICAL PRODUCTS, INC. WORCESTER, MASS. U.S.A.

*U.S. Patent No. 2,441,498

The blood-building,
appetite-building
iron tonic
with B_{12} activity
plus . . . iron (ferrous gluconate) in tonic quantities
plus . . . essential B complex vitamins well in excess of known minimum daily requirements
plus . . . pleasant taste, too
ELIXIR
CAPSULES
BETA-CONCEMIN FERRATED
IRON-B COMPLEX WITH B12 ACTIVITY
Beta-Concemin®
Merrell
1828
New York • CINCINNATI • Toronto

when other external therapy seems to get **nowhere...**

accelerate healing with

DESITIN®
OINTMENT
the pioneer external cod liver oil therapy

in **wounds**
(especially slow healing)
burns
ulcers
(decubitus, varicose, diabetic)

Study[1], after study[2] after study[3] corroborates the "notable"[1] success of Desitin Ointment in easing pain and stimulating smooth tissue repair in lacerated, denuded, chafed, irritated, ulcerated tissues—often in stubborn conditions where other therapy fails.

Protective, soothing, healing, Desitin Ointment is a non-irritating, blend of high grade, crude Norwegian cod liver oil (with its unsaturated fatty acids and high potency vitamins A and D in proper ratio for maximum efficacy), zinc oxide, talcum, petrolatum, and lanolin. Does not liquefy at body temperature and is not decomposed or washed away by secretions, exudate, urine or excrements. Dressings easily applied and painlessly removed. Tubes of 1 oz., 2 oz., 4 oz., and 1 lb. jars.

write for **samples** and literature

DESITIN CHEMICAL COMPANY
70 Ship Street, Providence 2, R. I.

1. Behrman, H. T., Combes, F. C., Bobroff, A., Leviticus, R.: Ind. Med. & Surg. 18:512, 1949.
2. Turell, R.: New York St. J.M. 50:2282, 1950.
3. Heimer, C. B., Grayzel, H. G., and Kramer B.: Archives Pediat. 68:382, 1951.

DIARRHEA OR DYSENTERY

Arobon®

meets the patient's first demand

In diarrheas, Arobon assures rapid control of the abdominal distress, the frequent stools, and the resulting generalized discomfort.

Processed from specially prepared carob flour, Arobon contains a high proportion (22 per cent) of pectin, lignin, and hemicellulose. Its adsorptive and demulcent actions serve to remove offending bacteria and toxins, and the gelatinous mass it forms on taking up water soothes the inflamed bowel.

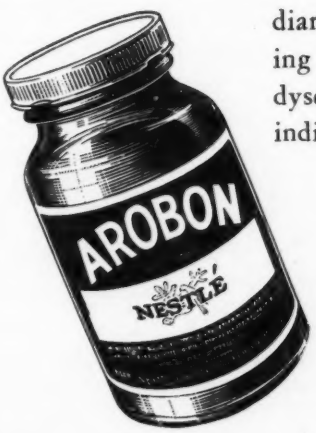
Arobon produces excellent results in the non-specific diarrheas of adults, children, and infants, often leading to formed stools in 12 to 15 hours. In the specific dysenteries, its action is valuable in conjunction with indicated chemotherapeutic agents.

SIMPLE TO PREPARE AND HIGHLY PALATABLE

For adults and children, Arobon is simply prepared by stirring the powder into milk. Average dose for adults, two level tablespoonfuls in four ounces; for children, one level tablespoonful in four ounces.

For infants, two level teaspoonfuls in four ounces of skim milk or water and boiled for ½ minute.

When mixed with milk, Arobon forms a pleasant chocolate-like drink.



Available in five ounce bottles through all pharmacies

THE NESTLÉ COMPANY, INC.

COLORADO SPRINGS, COLORADO

"TINEA CAPITIS . . ."

SPERSOL (DOAK)

Tetrachlor-P-Benzoquinone (SPERGON) in carbowax. Available in 5%, 10% and 20% concentration.

SPERSOL (DOAK) is greaseless, stainless, odorless. Easily removed with water.

Indication: Ringworm of the Scalp (Microsp. Audouini or Lanosum)
Suggested Method of Treatment: Hair must be clipped every 10 days. Rub Spersol into the scalp nightly.

In 4 oz., 1 lb. and 5 lb. containers.

Clinical Samples on Request

DOAK COMPANY, INC.

15812 Waterloo Road, Cleveland 10, Ohio

Continued from page 42

a $6,966 research grant by the American Cancer Society for the study on "Nutrition and the Alarm Response in Cancer Patients."

Dr. Charles H. Eades, Jr., assistant professor of chemistry, University of Tennessee Medical Units, Memphis, has been awarded a $4,670 research grant by the Office of Naval Research, United States Navy.

University of Tennessee Medical Units, Memphis, has been awarded a $16,163 grant by the Atomic Energy Commission for a physiologist to study the effects of radiation on certain body processes. Dr. R. R. Overman, associate professor, will conduct the investigation.

Dr. Albert Moore Hand, Texarkana, Texas, has been appointed instructor in the Divisions of Pediatrics and Preventive Medicine, University of Tennessee College of Medicine, Memphis, effective July 1.

TEXAS

Construction of a $3,250,000 building at the Southwestern Medical School of the University of Texas, Dallas, is scheduled to begin within the next few months.

Texas Association of Obstetricians and Gynecologists, at the twenty-third annual meeting, installed Dr. George F. Adam, Houston, president; and elected Dr. D. D. Wall, San Angelo, president-elect; Dr. Landon C. Arnim, Corpus Christi, vice-president; and Dr. Carey Hiett, Fort Worth, secretary-treasurer.

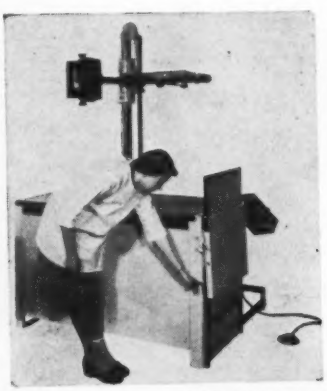
Southwest Allergy Forum at its annual meeting held recently in Dallas elected Dr. Orval R. Withers, Kansas City, Missouri, president; and Dr. James Holman, Dallas, secretary-treasurer.

University of Texas Medical Branch Library has been donated the library of the late Dr. Malcolm Kelly McCullough, Dallas.

Dr. David W. Carter, Jr., Dallas, has been named to fill an unexpired term on the State Board of Education.

Dr. Helen Clark, Paris, has been awarded a postdoctoral research fellowship by the Life Insurance Medical Research Fund to carry on research under the guidance of Dr. E. E. Muirhead at Southwestern Medical School, Dallas.

Continued on page 48



the

mattern

MINIMAX

combination examination table and x-ray unit

The Mattern Minimax offers maximum versatility and requires only a minimum investment —a particularly good combination for the general practitoner.

The Minimax presents these outstanding advantages:

- **Requires no special installation —takes no more space than an ordinary examination table alone. Serves as examination table with stirrups and pads.**
- **Permits horizontal and vertical radiography and fluoroscopy— with change-overs effected by merely tripping a panel release.**
- **Needs almost no servicing— since its sturdy dependability insures long-term, trouble-free operation. Requires less assistance to use; lets you give your full attention to the patient.**
- **Includes such diversified advantages of modern equipment design as telescoping panel for vertical fluoroscopy of adults, with horizontal extension for children.**
- **Integrally built lead shutters, shockproof vacuum sealed tube-head, fine focal spot, and overall neat, professional appearance.**

for utmost practicality

20MA UNIT

$1535

F.O.B. CHICAGO

MATTERN X-RAY

Write for our illustrated Bulletin No. 142.

F. MATTERN MFG. CO.

See your local Mattern dealer, or write direct to us for information.

4635-4659 NORTH CICERO AVENUE • CHICAGO 30, ILLINOIS

"Malnutrition can exist on 3 square meals daily"

Neal, M. P.: Diagnostic Drifts, Deceptions and Common Misses. J. A. M. A., 146:539 (June 9) 1951.

Nutrient deficient foodstuffs

Lengthy storage

Poor processing

Faulty preparation

Extensive clinical investigations have proved that optimal health and well-being demands the daily supplementation of all essential nutrients including Vitamins, Minerals, and Trace Elements—the factors which are NOW known to be essential components of the vital enzyme systems which control all metabolic activity.

VITERRA provides balanced amounts of 10 Vitamins, including Vitamin B_{12}, and 11 Minerals and Trace Elements, for more dependable protection against inadequacies of the daily diet.

Wherever more effective vitamin-mineral therapy is indicated . . . Specify

Viterra

Available at all Pharmacies in bottles of 100 capsules.

EACH CAPSULE CONTAINS:

Vitamin A	5,000 U.S.P. Units
Vitamin D	500 U.S.P. Units
Vitamin B_{12}	1 mcg.
Thiamine Hydrochloride	3 mg.
Riboflavin	3 mg.
Pyridoxine Hydrochloride	0.5 mg.
Niacinamide	25 mg.
Ascorbic Acid	50 mg.
Calcium Pantothenate	5 mg.
Mixed Tocopherols (Type IV)	5 mg.
Calcium	213 mg.
Cobalt	0.1 mg.
Copper	1 mg.
Iodine	0.15 mg.
Iron	10 mg.
Manganese	1 mg.
Magnesium	6 mg.
Molybdenum	0.2 mg.
Phosphorus	165 mg.
Potassium	5 mg.
Zinc	1.2 mg.

J. B. ROERIG AND COMPANY • 536 LAKE SHORE DR., CHICAGO 11, ILLINOIS

Continued from page 46

Dr. John Chapman, Dallas, has been named to the school board of the Highland Park School District to fill the unexpired term of the late Dr. J. Shirley Hodges.

Southwestern Surgical Congress will meet in Dallas, October 20-22, under the presidency of Dr. Leo J. Starry, Oklahoma City, Oklahoma.

Southwest Regional Cancer Conference will be held in Fort Worth, September 25.

Texas Pediatric Society will meet in Dallas, October 17-18, under the presidency of Dr. C. S. E. Touzel, Fort Worth.

VIRGINIA

Medical Society of Virginia will hold its next meeting in Richmond, September 28-October 1.

The Twenty-Fifth Annual Spring Congress of the Gill Memorial Eye, Ear, and Throat Hospital, held in Roanoke, April 7-12, was its Silver Anniversary. The attendance was the largest in the history of the Congress.

Dr. Elbyrne G. Gill, Roanoke, was elected president of the Alumni Association of the New York Eye and Ear Infirmary, and also a member of the Board of Directors of the Hospital, at the annual meeting of the association held in New York City, April 22-24.

Tri-State Medical Association of the Carolinas and Virginia, at its recent meeting, installed Dr. James Asa Shield, Richmond, president; and elected Dr. Grady Dixon, Ayden, North Carolina, president-elect; Dr. Paul D. Camp, Richmond, Dr. J. K. Webb, Greenville, South Carolina, and Dr. A. Burke Suitt, Durham, North Carolina, vice-presidents; and Dr. R. B. Davis, Greensboro, North Carolina, secretary-treasurer.

Dr. James W. Fullerton has been appointed health officer of the Buchanan-Tazewell Health District.

Dr. C. T. Wilfong has opened an office in Richmond for the practice of neurology and psychiatry.

Dr. Isaac C. East has resigned a position he has held for several years as clinical director of Eastern State Hospital, Williamsburg, to accept the superintendency of Spencer State Hospital, Spencer, West Virginia. Dr. East is succeeded by Dr. Eleanor Beamer-Maxwell, who has been with the Williamsburg Hospital for ten years, serving as chief of the woman's division.

Major faculty promotions at Medical College of Virginia, Richmond, are: Dr. Erling S. Hegre, to professor of anatomy; Dr. H. Wallace Blanton, associate professor of clinical medicine; Dr. Edward S. Ray, associate professor of medicine; Dr. William R. Kay, Dr. Arthur Klein, Dr. Howard McCue, and Dr. J. Warrick Thomas, assistant professors of clinical medicine; Dr. Charles E. Troland, professor of clinical neurological surgery; Dr. William Durwood Suggs, associate professor of clinical obstetrics; Dr. Edwin L. Kendig, Jr., and Dr. Carolyn McCue, assistant professors, of pediatrics; Dr. Patrick H. Drewry, Jr., professor of psychiatry; Dr. Merritt W. Foster, Jr., and Dr. Lucy S. Hill, assistant professors of psychiatry; Dr. A. Ray Dawson, associate professor of clinical physical medicine and rehabilitation; Dr. Edward M. Holmes, Jr., professor of community medicine; Dr. Paul W. Bowden, associate professor of community medicine; Dr. Hunter B. Frischkorn, Jr., and Dr. George A. Welchons, assistant professors of clinical radiology; Dr. Saul Kay, professor of surgical pathology; Dr. Leroy Smith, associate professor of clinical surgery; and Dr. R. S. Siersema, assistant professor of clinical surgery.

Dr. Daniel D. Talley, for many years professor of clinical radiology at the Medical College of Virginia, Richmond, has been named emeritus professor of clinical radiology.

WEST VIRGINIA

West Virginia State Medical Association will hold its 85th annual meeting in White Sulphur Springs, The Greenbrier, July 24-26.

Dr. Julian R. Kaufman, formerly of Charleston, is chief of medical services, Veterans Administration Hospital, Miles City, Montana.

Dr. Milton O. Beebe, Jr., Thorpe, has moved to Maybeury where he will continue in general practice.

Dr. Thomas G. Reed, Charleston, a past president of the West Virginia State Medical Association, has been named a member of the Executive Board of the new Medical-Service Plan, Inc., a non-profit collection plan for doctors, dentists and hospitals.

Aminophyllin . . .

a "most effective single agent for prompt relief" of severe **bronchial asthma**

"useful as a peripheral vasodilator and myocardial stimulant" in

pulmonary edema
paroxysmal dyspnea of congestive heart failure
Cheyne-Stokes respiration

H. E. DUBIN LABORATORIES, INC.
250 E. 43rd St. • New York 17, N. Y.

dubin
aminophyllin
(theophylline-ethylenediamine)

readily soluble for rapid therapeutic effect.

TABLETS • AMPULS
POWDER
SUPPOSITORIES

BRAWNER'S SANITARIUM

Established 1910
Smyrna, Georgia (Suburb of Atlanta)

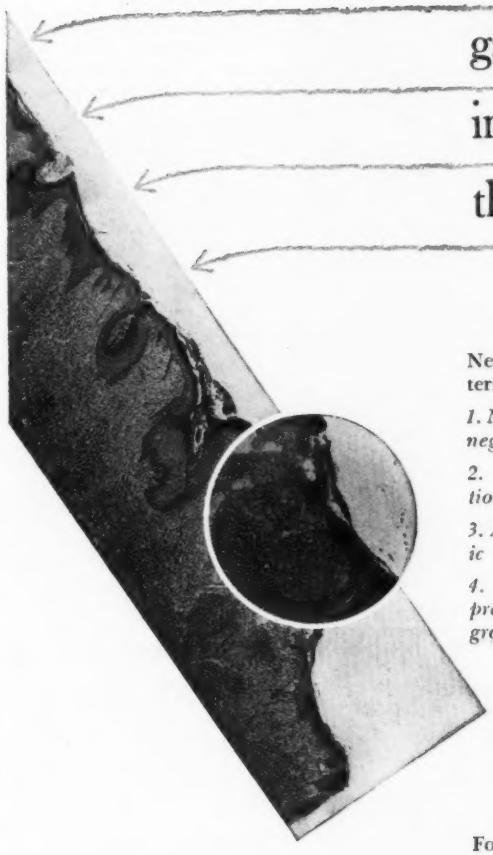
FOR THE TREATMENT OF

Nervous and Mental Illnesses, Drug and Alcohol Addictions

JAS. N. BRAWNER, M.D., Medical Director

ALBERT F. BRAWNER, M.D., Dept. for Men JAS. N. BRAWNER, JR., M.D., Dept. for Women

four-way
gain
in topical
therapy



Neomycin is a new wide-range antibiotic for external use against skin infections.

1. Neomycin is highly effective against both Gram-negative and Gram-positive organisms.

2. The incidence of sensitization (allergic) reactions to neomycin is extremely low.

3. Absorption of neomycin is negligible, so systemic toxic side effects are substantially eliminated.

4. Neomycin retains antibacterial potency in the presence of exudates and products of bacterial growth.

Neomycin

For therapy of specific or mixed cutaneous infections —

Myciguent Ointment — 5 mg. per Gm., in ½ oz. tubes; 1 oz. tubes; and 4 oz. jars.*

For rapid control of eye infections —

Myciguent Ophthalmic Ointment — 5 mg. per Gm., in 1 drachm tubes.*

For preparation of solutions for topical use only —

Neomycin Sulfate, Sterile Powder — Vials containing 0.5 Gm.

*Trademark

a product of **Upjohn Research** *for medicine . . . produced with care . . . designed for health*

THE UPJOHN COMPANY, KALAMAZOO, MICHIGAN

One of America's Fine Institutions . . . .

Newdigate M. Owensby, M.D.
Psychiatrist-in-Chief
Specialist Certified by the American Board of Psychiatry and Neurology

Willis T. McCurdy, M.D.
Attending Physician

J. Rufus Evans, M.D.
Attending Physician

Elizabeth Hancock
Psycho-Therapist

Atlanta Office
384 Peachtree Street

Dedicated to the Scientific Treatment of Nervous and Mental Disorders . . .
. . In a Setting of Inviting Friendliness and Simple Grace . . Elevation 1200 Feet

BROOK HAVEN MANOR SANITARIUM
STONE MOUNTAIN, GA.

From Our

WESTBROOK PORTFOLIO

A private psychiatric sanatorium employing modern diagnostic and treatment procedures—electro shock, insulin, psychotherapy, occupational and recreational therapy—for nervous and mental disorders and problems of addiction.

This view of the Administration Building is typical of the restful beauty of the Westbrook 125-acre estate.

WESTBROOK SANATORIUM

Staff: PAUL V. ANDERSON, M.D., President; JOHN R. SAUNDERS, M.D., Associate; REX BLANKINSHIP, M.D., Medical Director; THOMAS F. COATES, M.D., Associate

P. O. Box 1514 RICHMOND, VIRGINIA Phone 5-3245

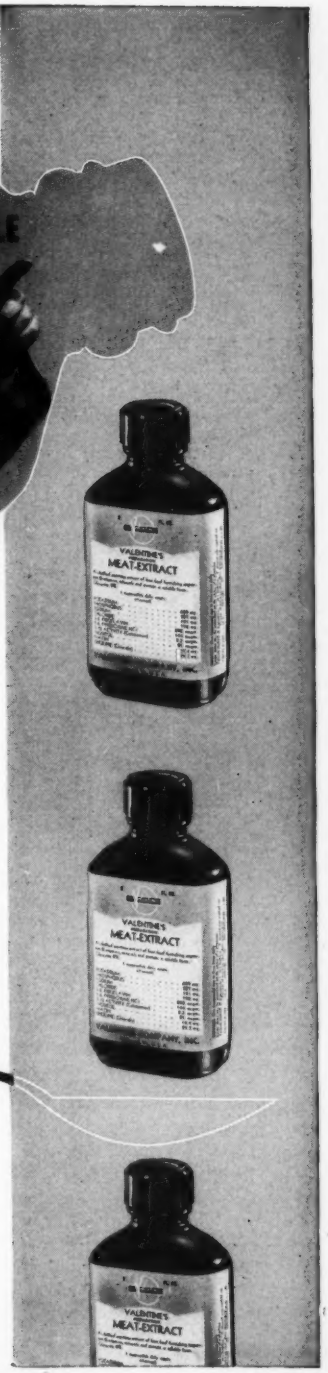
OLD AGE BENEFITS

VALENTINE'S MEAT EXTRACT

HAS SPECIAL VALUE FOR THE AGED AND AGING, PROVIDING:

the psychologic benefits of a "tonic", plus
the physiologic benefits derived from

- stimulation of failing appetites
- increased flow of digestive fluids
- supplementary amounts of vitamins, minerals and soluble proteins
- extra-dietary vitamin B_{12}
- protective quantities of potassium in a palatable and readily assimilated form



Supplied in bottles of 2 fluidounces.

DOSAGE: One teaspoonful two or three times daily. Two or three times this amount may be prescribed for potassium therapy.

VALENTINE COMPANY, INC.

RICHMOND 9, VIRGINIA

APPALACHIAN HALL

ASHEVILLE, NORTH CAROLINA

An institution for rest, convalescence, the diagnosis and treatment of nervous and mental disorders, alcohol and drug habituation.

Appalachian Hall is located in Asheville, North Carolina. Asheville justly claims an unexcelled all year round climate for health and comfort. All natural curative agents are used, such as physiotherapy, occupational therapy, shock therapy, outdoor sports, horseback riding, etc. Five beautiful golf courses are available to patients. Ample facilities for classification of patients. Rooms single or en suite with every comfort and convenience.

For rates and further information write **Appalachian Hall, Asheville, N. C.**

Wm. Ray Griffin, M.D. M. A. Griffin, M.D.

STUART CIRCLE HOSPITAL

413-21 Stuart Circle

RICHMOND 20, VIRGINIA

Medicine:
ALEXANDER G. BROWN, JR., M.D.
MANFRED CALL, III, M.D.
M. MORRIS PINCKNEY, M.D.
ALEXANDER G. BROWN, III, M.D.
JOHN D. CALL, M.D.

Obstetrics and Gynecology:
WM. DURWOOD SUGGS, M.D.
SPOTSWOOD ROBINS, M.D.

Orthopedics:
BEVERLEY B. CLARY, M.D.

Pediatrics:
CHARLES P. MANGUM, M.D.
ALGIE S. HURT, M.D.

Ophthalmology, Otolaryngology:
W. L. MASON, M.D.

Pathology:
REGENA BECK, M.D.

Bacteriology:
FORREST SPINDLE

Surgery:
A. STEPHENS GRAHAM, M. D.
CHARLES R. ROBINS, JR., M.D.
CARRINGTON WILLIAMS, M.D.
RICHARD A. MICHAUX, M.D.
CARRINGTON WILLIAMS, JR., M.D.

Urological Surgery:
FRANK POLE, M.D.

Oral Surgery:
GUY R. HARRISON, D.D.S.

Roentgenology and Radiology:
FRED M. HODGES, M.D.
L. O. SNEAD, M.D.
HUNTER B. FRISCHKORN, JR., M.D
WILLIAM C. BARR, M.D.

Physiotherapy:
IRMA LIVESAY

Director:
CHARLES C. HOUGH

tastes like **candy**

kids say it's **dandy**

new, **aqueous** vitamin syrup

Normally oil-soluble vitamins A and D in this potent multivitamin syrup are in aqueous form—for more rapid, more complete, and more assured absorption and utilization.

No bribe, no threat, no coaxing—because children love the delicious, candy-like flavor of new VI-AQUA SYRUP. They ask for it . . . take it right from the spoon . . . or can be mixed with milk, formula, juices, cereals, etc.

VI-AQUA syrup

AQUEOUS . . . for more certain absorption and better utilization

Each 5 cc. (approx. 1 teaspoonful) provides:

VITAMIN A*	4,000 U.S.P. Units
VITAMIN D*	800 U.S.P. Units
THIAMINE HCl (B_1)	1.5 mg.
RIBOFLAVIN (B_2)	1.2 mg.
NIACINAMIDE	10 mg.
PYRIDOXINE HCl (B_6)	0.3 mg.
PANTHENOL (pantothenic acid equiv.)	2 mg.
ASCORBIC ACID (C)	50 mg.

*Oil-soluble vitamin A and natural vitamin D made water-soluble with sorethytan esters; protected by U. S. Patent 2,417,299. Contains no alcohol.

Supplied in 4 oz., 16 oz. and gallon bottles.

Send for tasting samples.

U. S. VITAMIN CORPORATION
CASIMIR FUNK LABORATORIES, INC. (affiliate)
250 EAST 43rd ST., NEW YORK 17, N. Y.

CITY VIEW SANITARIUM

For the diagnosis and treatment of nervous and mental disorders, and addictions to alcohol and drugs.

Established 1907

NASHVILLE, TENNESSEE

St. Elizabeth's Hospital

Richmond 20, Virginia

STAFF

Guy W. Horsley, M.D.	General Surgery & Gynecology
Leroy Smith, M.D.	Plastic and General Surgery
D. Coleman Booker, M.D.	General Surgery & Gynecology
Austin I. Dodson, M.D.	Urology
William J. Frohbose, M.D.	Urology
Douglas G. Chapman, M.D.	Internal Medicine
Elmer S. Robertson, M.D.	Internal Medicine
Fred M. Hodges, M.D.	Roentgenology
L. O. Snead, M.D.	Roentgenology
Hunter B. Frischkorn, Jr., M.D.	Roentgenology
Randal A. Boyer, M.D.	Roentgenology
George E. Snider, M.D.	Internal Medicine
Helen Lorraine	Medical Illustration

Administration

WILLIAM SCOTT, Business Manager

The operating rooms and all of the front bedrooms are completely air-conditioned.

School of Nursing

The School of Nursing is affiliated with The Johns Hopkins Hospital School of Nursing for a three-months' course each in Pediatrics and Obstetrics.

Address: Director of Nursing Education

Saint Albans Sanatorium

RADFORD, VIRGINIA

100 bed private psychiatric hospital for the treatment of nervous and mental disorders, including alcoholism and addiction.

James P. King, M.D.
Director

James K. Morrow, M.D.
Thomas E. Painter, M.D.

Daniel D. Chiles, M. D.
Wendell T. Wingett, M.D.

James L. Chitwood, M.D.
Medical Consultant

To combat intestinal and extra-intestinal amebiasis, found in every state of the Union:

MILIBIS® because of relative insolubility, assures high concentration in the large intestine, very effective against subacute and chronic amebiasis. Average adult dose: 0.5 Gm. (1 tablet) three times daily for 7 to 10 days, repeated if necessary. Control acute dysentery first or concurrently with emetine.

Supplied in 0.5 Gm. tablets, bottles of 25.

ARALEN® Diphosphate —the well known antimalarial—induces *complete clinical remission* in pleuropulmonary amebiasis[1] as well as hepatic and other forms of extra-intestinal amebiasis.[2,3] Average adult dose: 1 Gm. (4 tablets) daily for 2 days, then 0.5 Gm. daily for 2 to 3 weeks, which may be combined with or successive to Milibis therapy of intestinal amebiasis.

Supplied in 0.25 Gm. tablets, bottles of 100 and 1000.

Milibis and Aralen, trademarks reg. U. S. & Canada, brand of bismuth glycolylarsanilate and chloroquine, respectively.

1. Lindsay, A. E., Gossard, W. H., and Chapman, J. S.: *Dis. Chest*, 20:533, Nov., 1951.
2. Conan, N. J., Jr.: *Am. Jour. Med.*, 6:309, Mar., 1949.
3. Emmett, J.: *J.A.M.A.*, 141:22, Sept. 3, 1949.

Illustrated brochure on request.

WINTHROP-STEARNS INC.
New York 18, N. Y. Windsor, Ont.

TUCKER HOSPITAL, INC.

212 West Franklin St. (Corner of Madison)

RICHMOND, VIRGINIA

This is a private Hospital for the Neurological Practice of Drs. Beverly R. Tucker, Howard R. Masters and James Asa Shield.

The Tucker Hospital is for the treatment of nervous and endocrine diseases. There are departments of massage, medicinal exercises, hydrotherapy and physiotherapy. The Hospital is large and bright, surrounded by a lawn and shady walks, large verandas and has a roof garden. It is situated in the best part of Richmond and is thoroughly and modernly equipped. The nurses are specially trained in the care of nervous cases.

Allen's
INVALID HOME

ESTABLISHED 1890

MILLEDGEVILLE, GEORGIA

For the treatment of

NERVOUS AND MENTAL DISEASES

Grounds 600 Acres — Buildings, Brick
Fireproof — Comfortable — Convenient

Site High and Healthful

E. W. ALLEN, M.D. — DEPARTMENT FOR MEN

H. D. ALLEN, M.D. — DEPARTMENT FOR WOMEN

Terms Reasonable

HILL CREST SANITARIUM

FOR NERVOUS AND MENTAL DISEASES AND ADDICTIONS

Insulin and Electro-Shock Therapy used in Selected Cases. Gradual Reduction Method used in the Treatment of Addictions.
Established in 1925

Thoroughly modern in architecture and construction. Eight departments—affording proper classification of patients. All outside rooms, attractively furnished. Several bathrooms and rooms with private bath on each floor. Also a spacious sun parlor in each department. Located on the crest of Higdon Hill, 1050 feet above sea level, overlooking the city, and surrounded by an expanse of beautiful woodland. Ample provision made for diversion and helpful occupation. Adequate night and day nursing service maintained.

James A. Becton, M.D., Physician-in-charge — James Keene Ward, M.D., Associate Physician

P. O. Box 2896, Woodlawn Station, Birmingham 6, Ala. — Phones 9-1151 and 9-1152

CARROL TURNER SANATORIUM

MEMPHIS, TENNESSEE, ROUTE 10, BOX 288

For the Diagnosis and Treatment of Mental and Nervous Diseases

Located on the Raleigh-LaGrange Road, five miles east of the city limit —accessible to U. S. Highway 70 (Bristol Highway)

Situated on a sixty-six acre tract of wooded land and rolling fields, the environment is conducive to amelioration of the symptoms of emotionally disturbed patients

Modernly equipped with adequate facilities for physical and hydrotherapy, electroshock, and insulin therapy

Special emphasis is laid on recreational and occupational therapy

Adequate nursing personnel assures individual attention to each patient

The main building and hospital department of the Sanatorium is shown above

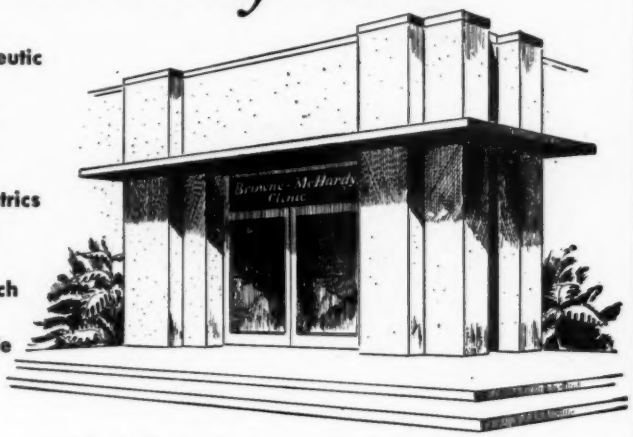
FAIRFIELD

Our convalescent home is located on the Sanatorium Grounds

The home is especially designed and fitted for the care of elderly people.

Browne-McHardy Clinic

- Diagnostic and Therapeutic Facilities
- Internal Medicine and Gastroenterology
- Surgery
- Gynecology and Obstetrics
- Radiology—X-ray and Radium therapy
- Laboratory and Research Departments
- Hotel facilities available



3636 ST. CHARLES AVENUE

Phone UPtown 9580 • *New Orleans, La.*

THE WALLACE SANITARIUM

Memphis, Tennessee

For the Diagnosis and Treatment of Nervous and Mental Diseases, Drug Addiction and Alcoholism.

FIFTH ANNUAL

Postgraduate Assembly

in

ENDOCRINOLOGY AND METABOLISM

Sponsored by

THE ENDOCRINE SOCIETY

Roney Plaza Hotel

Miami Beach, Florida **November 3-8, 1952**

The faculty will consist of 20 clinicians and investigators eminently qualified in the fields of endocrinology and metabolism.

The program will consist of lectures, clinics, laboratory demonstrations and scientific exhibits.

The 64 lectures to be presented will cover all phases of endocrinology and metabolic disorders. Ample time will be given for discussions and answers at the end of each session and registrants are encouraged to contact members of the faculty for individual discussions. The entire program has been designed to interest not only the specialist but those in general practice and has been approved by the American Academy of General Practice for postgraduate credit.

A simultaneous translation of all lectures into Spanish will be provided through earphones.

Copies of the proceedings of the Assembly will be available to all registrants.

The Roney Plaza with its tropical gardens, outdoor swimming pool, putting greens, private beach and Cabana Club, has long been recognized as one of Florida's great beach hotels and offers special convention rates to members of this Assembly. The Surf Room, in which the sessions will be held, is delightfully air conditioned and has subdued lighting which permits taking of notes and viewing lantern slides with comfort.

A fee of $75 will be charged for the entire course and the attendance will be limited to 200. REGISTRATION WILL BE IN THE ORDER OF CHECKS RECEIVED AND WILL CLOSE ON OCTOBER 3, 1952. Should there be an insufficient number of applicants to fill the course, the registration fee will be refunded immediately in its full amount.

Please forward application on your letterhead, together with check payable to The Endocrine Society, to Henry H. Turner, M.D., Secretary-Treasurer, 1200 North Walker Street, Oklahoma City 3, Oklahoma, before October 3, 1952. Further information and program will be furnished upon request.

Hotel reservations should be made directly with the Roney Plaza Hotel, Miami Beach, Florida, and the hotel advised that you are attending this Postgraduate Assembly.

SUPERIOR VITAMIN SUPPLEMENTS

for their varying vitamin needs

MEAD'S 3 *versatile* "VI-SOLS"

Pleasant tasting . . .
superior flavors assure patient acceptance

Clear, light texture . . .
non-sticky; flow easily from dropper

Exceptional dispersibility . . .
disperse instantly in fruit juice or water; mix readily with formula

Highly stable . . .
stable at room temperature; may be autoclaved with formula

Easy, accurate dosage measurement . . .
specially designed, easy-to-read dropper assures accurate dosage

Convenient . . .
may be given in formula, fruit juice or water, or dropped into mouth

	Vitamin A	Vitamin D	Ascorbic Acid	Thiamine	Riboflavin	Niacinamide
POLY-VI-SOL Each 0.6 cc. supplies	5000 Units	1000 Units	50 mg.	1 mg.	0.8 mg.	5 mg.
TRI-VI-SOL Each 0.6 cc. supplies	5000 Units	1000 Units	50 mg.			
CE-VI-SOL Each 0.5 cc. supplies			50 mg.			

MEAD'S MEAD JOHNSON & CO. • EVANSVILLE 21, IND., U. S. A.

QUOTANE*

...topical anesthetic

in "summer dermatoses"

Poison Ivy	**Sunburn**
Athlete's Foot	**Insect Bites**
Prickly Heat	**Contact Dermatitis**

• 'Quotane' provides immediate and prolonged relief in the long list of itching and burning conditions so common in spring and summer.

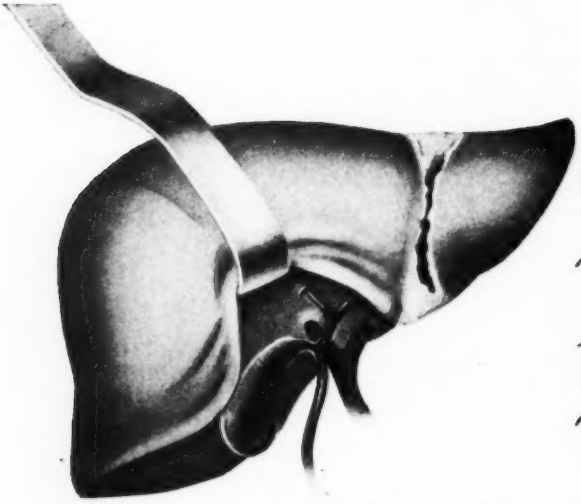
• 'Quotane'—as demonstrated in extensive clinical trials—is virtually non-sensitizing.

'QUOTANE' OINTMENT—for dry lesions

'QUOTANE' LOTION—for moist lesions

Smith, Kline & French Laboratories, Philadelphia

*Trademark for 1-(β-dimethylaminoethoxy)-3-n-butylisoquinoline hydrochloride, S.K.F.



to restore *normal fat metabolism*

HEPA-DESICOL

TRADE MARK

Kapseals®

combined lipotropic and bile therapy

HEPA-DESICOL combines choline, methionine, and inositol with Desicol (desiccated whole fresh bile, Parke-Davis). It is valuable in the treatment of liver dysfunction often accompanying early cirrhosis, alcoholism, diabetes mellitus, malnutrition, obesity, and atherosclerosis.

Lipotropic action of choline, methionine, and inositol is well established; Desicol not only provides additional bile but also stimulates normal bile flow. This dual action of **HEPA-DESICOL** provides more effective therapy of disturbed fat metabolism.

HEPA-DESICOL Kapseals are supplied in bottles of 100 and 1000.

each Kapseal contains:

dl-Methionine	150 mg.
Choline Bitartrate	200 mg.
Inositol	50 mg.
Desicol®	150 mg.

dosage – Two to four Kapseals three times a day, with or immediately following meals.

MEDICAMENTA VERA

Parke, Davis & Company

DETROIT, MICHIGAN